

Pyelonephritis (acute): antimicrobial prescribing

NICE guideline

Draft for consultation, May 2018

This guideline sets out an antimicrobial prescribing strategy for acute pyelonephritis (upper urinary tract infection). It aims to optimise antibiotic use and reduce antibiotic resistance.

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

Who is it for?

- Health professionals
- People with acute pyelonephritis, 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

The recommendations in this guideline are for managing acute pyelonephritis (also called upper urinary tract infection [UTI]) in adults, young people and children who do not have a catheter.

1.1 *Managing acute pyelonephritis*

- 1.1.1 Be aware that acute pyelonephritis is an infection of one or both kidneys usually caused by bacteria travelling up from the bladder.
- 1.1.2 Give advice about managing symptoms with self-care (see the recommendations on [self-care](#)) to all people with acute pyelonephritis.

Treatment for acute pyelonephritis

- 1.1.3 In people aged 16 years and over with acute pyelonephritis obtain a midstream urine sample before prescribing antibiotics and send for culture and susceptibility testing.
- 1.1.4 In children and young people under 16 years with acute pyelonephritis obtain a midstream urine sample before prescribing antibiotics and send for culture and susceptibility testing in line with the NICE guideline on [urinary tract infection in under 16s: diagnosis and management](#).
- 1.1.5 Assess and manage children under 5 with acute pyelonephritis who present with fever as outlined in the NICE guideline on [fever in under 5s](#).
- 1.1.6 Offer an antibiotic (see the recommendations on [choice of antibiotic](#)) to people with acute pyelonephritis. Take account of:
- the severity of symptoms
 - the risk of developing complications, which is higher in people with known or suspected structural or functional abnormality of the genitourinary tract or underlying disease (such as diabetes or immunosuppression)
 - previous urine culture and susceptibility results
 - previous antibiotic use which may have led to resistant bacteria.

1.1.7 When results of urine cultures are available:

- review the choice of antibiotic, **and**
- change the antibiotic according to susceptibility results if the bacteria are resistant, using narrow spectrum antibiotics wherever possible.

Advice when an antibiotic prescription is given

1.1.8 When an antibiotic is given, as well as the general advice on [self-care](#), give advice about:

- possible adverse effects of the antibiotic, particularly diarrhoea and nausea
- seeking medical help if symptoms worsen rapidly or significantly at any time, do not start to improve within 48 hours of taking the antibiotic, or the person becomes systemically very unwell.

Reassessing symptoms

1.1.9 Reassess if symptoms worsen rapidly or significantly at any time, or do not start to improve within 48 hours of taking the antibiotic, taking account of:

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

Referring to hospital

- 1.1.10 Refer people aged 16 years and over with acute pyelonephritis to hospital if they have a severe systemic infection (any of the high risk criteria from the NICE guideline on [sepsis](#)).
- 1.1.11 Consider referring people aged 16 years and over with acute pyelonephritis to hospital if they:
- are significantly dehydrated or unable to take oral fluids and medicines, **or**
 - are pregnant, **or**
 - have a higher risk of developing complications (for example, people with known or suspected structural or functional abnormality of the genitourinary tract or underlying disease [such as diabetes or immunosuppression]).
- 1.1.12 Refer children and young people with acute pyelonephritis to hospital in line with the NICE guideline on [urinary tract infection in under 16s: diagnosis and management](#).

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

1.2 Self-care

- 1.2.1 Consider paracetamol for pain in people with acute pyelonephritis.
- 1.2.2 Advise people with acute pyelonephritis about the adequate intake of fluids.

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

1.3 Choice of antibiotic

- 1.3.1 When prescribing antibiotic treatment for acute pyelonephritis:
- follow table 1 for non-pregnant women and men aged 16 years and over
 - follow table 2 for pregnant women aged 12 years and over

- follow table 3 for children and young people under 16 years.

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

1.3.3 Review intravenous antibiotics by 48 hours and consider stepping down to oral antibiotics where possible.

Table 1. Antibiotics for non-pregnant women and men aged 16 years and over

Antibiotic ¹	Dose and course length
First choice oral antibiotic²	
Co-amoxiclav	625 mg three times a day for 7 days
Ciprofloxacin	500 mg twice a day for 7 days
Levofloxacin	500 mg once a day for 7 days
Trimethoprim (only if culture results available and susceptible)	200 mg twice a day for 14 days
First choice intravenous antibiotic (if vomiting, unable to take oral antibiotics, or severely unwell). Antibiotics may be combined if sepsis a concern^{2,3}	
Co-amoxiclav	1.2 g three times a day
Ciprofloxacin	400 mg twice or three times a day
Ceftriaxone	1 to 2 g once a day
Gentamicin	5 mg/kg to 7 mg/kg once a day
Amikacin	15 mg/kg once a day
Second choice intravenous antibiotic if higher risk of developing resistance^{2,3}	
Consult local microbiologist	
¹ See BNF for appropriate use and dosing in specific populations, for example, hepatic impairment, renal impairment and breast-feeding.	
² Check any previous urine culture and susceptibility results and antibiotic prescribing and choose antibiotics accordingly.	
³ Review intravenous antibiotics by 48 hours and consider stepping down to oral antibiotics where possible for a total antibiotic course of 7 days.	

Table 2. Antibiotics for pregnant women aged 12 years and over

Antibiotic ¹	Dose and course length
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First choice oral antibiotic²	
Cefalexin	500 mg twice or three times a day for 7 days
First choice intravenous antibiotic (if vomiting, unable to take oral antibiotics, or severely unwell)^{2,3}	
Cefuroxime	750 mg three or four times a day
Second choice intravenous antibiotic if higher risk of developing resistance^{2,3}	
Consult local microbiologist	
<p>¹See BNF for appropriate use and dosing in specific populations, for example, hepatic impairment and renal impairment.</p> <p>²Check any previous urine culture and susceptibility results and antibiotic prescribing and choose antibiotics accordingly.</p> <p>³Review intravenous antibiotics by 48 hours and consider stepping down to oral antibiotics where possible for a total antibiotic course of 7 days.</p>	

Table 3. Antibiotics for children and young people under 16 years

Antibiotic¹	Dosage and course length²
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 oral antibiotic³	
Co-amoxiclav	<p>3 to 11 months, 0.25 ml/kg of 125/31 suspension three times a day for 7 to 10 days (dose doubled in severe infection)</p> <p>1 to 5 years, 5 ml of 125/31 suspension or 0.25 ml/kg of 125/31 suspension three times a day for 7 to 10 days (dose doubled in severe infection)</p> <p>6 to 11 years, 5 ml of 250/62 suspension or 0.15 ml/kg of 250/62 suspension three times a day for 7 to 10 days (dose doubled in severe infection)</p> <p>12 to 17 years, 250/125 mg three times a day or 500/125 mg three times a day for 7 to 10 days</p>
Cefalexin	<p>3 to 11 months, 125 mg or 12.5 mg/kg twice a day for 7 to 10 days</p> <p>1 to 4 years, 125 mg three times a day or 12.5 mg/kg twice a day for 7 to 10 days</p> <p>5 to 11 years, 250 mg three times a day for 7 to 10 days</p> <p>12 to 17 years, 500 mg twice or three times a day for 7 to 10 days</p>
First choice intravenous antibiotic (if vomiting, unable to take oral antibiotics or severely unwell). Antibiotics may be combined if sepsis a concern^{3,4,5}	

Co-amoxiclav	3 months to 17 years, 30 mg/kg three times a day (maximum 1.2 g three times a day)
Cefotaxime	50 mg/kg twice or three times a day (four times a day for severe infections; maximum 12 g per day)
Ceftriaxone	3 months to 11 years (up to 50 kg), 50 to 80 mg/kg once a day (maximum 4 g per day) 9 to 11 years (50 kg and above), 1 to 2 g once a day 12 to 17 years, 1 to 2 g once a day
Gentamicin	7 mg/kg once a day
Amikacin	15 mg/kg once a day
Second choice intravenous antibiotic if higher risk of developing resistance^{3,4,5}	
Consult local microbiologist	
<p>¹See BNF for children for appropriate use and dosing in specific populations, for example hepatic and renal impairment. See table 2 if the young woman is pregnant.</p> <p>²The 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.</p> <p>³Check any previous urine culture and susceptibility results and antibiotic prescribing and choose antibiotics accordingly.</p> <p>⁴Review intravenous antibiotics by 48 hours and consider stepping down to oral antibiotics where possible for a total of 10 days.</p> <p>⁵If intravenous treatment is not possible, consider intramuscular treatment.</p>	

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

Summary of the evidence

- The recommendations in this guideline are based on the evidence identified, which was mainly for people with acute pyelonephritis. Some studies also included people with a complicated urinary tract infection (associated with a structural or functional abnormality, or underlying disease, which increases the risk of a more serious outcome or treatment failure) or urosepsis (a systemic response to a urinary tract infection).

Self-care

- No systematic reviews or randomised controlled trials (RCTs) of any non-antimicrobial treatments were identified that met the inclusion criteria.

Committee discussion on self-care

- There was no evidence for the use of oral analgesia in acute pyelonephritis. However, paracetamol has a well-established efficacy and safety profile for managing pain and fever. The committee agreed that it was reasonable to consider paracetamol for managing pain and fever in adults, children and young people with acute pyelonephritis.
- Non-steroidal anti-inflammatory drugs, such as ibuprofen, are generally not recommended for people with acute pyelonephritis because of concerns about renal safety.
- Based on experience, the committee agreed that people should be advised about the adequate intake of fluids because maintaining full hydration is important in people with a UTI.

Antibiotics

- Acute pyelonephritis is a bacterial infection needing treatment with an antibiotic that reaches therapeutic concentrations in the kidney.
- Gram-negative bacteria are the most common causative pathogens in acute pyelonephritis, with *Escherichia coli* causing 60% to 80% of uncomplicated infections. Other gram-negative pathogens include *Proteus mirabilis* (responsible for about 15% of infections) as well as *Klebsiella* (approximately 20%), *Enterobacter* and *Pseudomonas* species. Less commonly, gram-positive bacteria such as *Enterococcus faecalis*, *Staphylococcus saprophyticus*, and *Staphylococcus aureus* may be seen.
- Complications of acute pyelonephritis include impaired renal function or renal failure, sepsis and preterm labour in pregnancy.

Choice of antibiotic

Efficacy of antibiotics

- Two randomised controlled trials (RCTs) ([Wagenlehner et al. 2015](#) and [Pasidechnikov et al. 2015](#)) compared an intravenous cephalosporin (ceftolozane/tazabactam or ceftazidime) with an intravenous quinolone (levofloxacin or ciprofloxacin) for acute pyelonephritis, acute obstructive

pyelonephritis or complicated urinary tract infection in adults. Moderate quality evidence found that ceftolozane/tazabactam was significantly more effective than levofloxacin for improving composite cure (clinical cure and microbiological eradication and microbiological cure; 76.9% versus 68.4%, number needed to treat [NNT] 12 [range 7 to 43]) but there was no significant difference between antibiotics for clinical cure. Ceftazidime had a significantly higher rate of clinical cure compared with ciprofloxacin (88.9% versus 73.8%; NNT 7 [range 4 to 62]; very low quality evidence).

- Two RCTs ([Park et al. 2012](#) and [Vasquez et al. 2012](#)) compared an intravenous cephalosporin (ceftriaxone or ceftazidime/avibactam) with an intravenous carbapenem (ertapenem or imipenem/cilastatin) for acute pyelonephritis or complicated urinary tract infection in adults. Very low to high quality evidence found that these cephalosporins and carbapenems were equally effective.
- Very low quality evidence from a small single RCT ([Moramezi et al. 2008](#)) in pregnant women with acute pyelonephritis found no significant difference between intravenous cephalothin and intravenous ampicillin plus gentamicin in the duration of lower UTI symptoms or costovertebral angle pain. The mean time to end of fever was reduced with ampicillin plus gentamicin compared with cephalothin (mean 11 hours lower, $p=0.01$; very low quality evidence).
- One RCT ([Peterson et al. 2008](#)) compared different quinolones (levofloxacin and ciprofloxacin: intravenous or oral) for acute pyelonephritis and complicated urinary tract infection in adults and found no significant differences in clinical or microbiological outcomes at follow-up (high quality evidence).
- One RCT ([Talan et al. 2000](#)) compared oral ciprofloxacin with oral co-trimoxazole for acute pyelonephritis in adult women. Low to moderate quality evidence found that ciprofloxacin was significantly more effective for clinical cure (96.5% versus 82.9%; NNT 8 [range 5 to 18]) and microbiological cure (99.1% versus 89.1%; NNT 10 [range 7 to 28]) than co-trimoxazole.

- Low quality evidence from 2 RCTs ([Wagenlehner et al. 2015](#) and Park et al. 2012) found no difference between antibiotics for the treatment of bacteraemia secondary to complicated urinary tract infection or acute pyelonephritis in adults.
- The evidence for children is based on 1 systematic review ([Strohmeier et al. 2014](#)) in acute pyelonephritis. No evidence from systematic reviews or RCTs was identified for children with complicated urinary tract infection. This systematic review did not find major differences in clinical effectiveness between different antibiotics compared in the studies (third and fourth generation cephalosporins, aminoglycosides, co-amoxiclav and co-trimoxazole; very low to moderate quality evidence).

Safety of antibiotics

- Antibiotic-associated diarrhoea occurs in 2 to 25% of people taking antibiotics, depending on the antibiotic used ([NICE Clinical Knowledge Summary \[CKS\]: diarrhoea – antibiotic associated](#)).
- Allergic reactions to penicillins occur in 1 to 10% of people and anaphylactic reactions occur in less than 0.05%. People with a history of atopic allergy (for example, asthma, eczema and hay fever) are at a higher risk of anaphylactic reactions to penicillins. People with a history of immediate hypersensitivity to penicillins may also react to cephalosporins and other beta-lactam antibiotics ([BNF, April 2018](#)). See the NICE guideline on [drug allergy: diagnosis and management](#) for more information.
- Trimethoprim has a teratogenic risk in the first trimester of pregnancy (folate antagonist; [BNF, April 2018](#)). Manufacturers advise contraindicated in pregnancy.
- Quinolones are generally not recommended in children or young people who are still growing ([BNF, April 2018](#)).
- Aminoglycosides doses are based on weight and renal function and whenever possible treatment should not exceed 7 days ([BNF, April 2018](#)).
- Overall there did not appear to be major differences in adverse effects between antibiotics based on the included studies, although these were not well reported (very low to low quality evidence).

- See the [summaries of product characteristics](#) for information on contraindications, cautions and adverse effects of individual medicines.

Committee discussion on choice of antibiotic

- Based on evidence and experience, the committee agreed that acute pyelonephritis is a bacterial infection needing treatment with antibiotics that reach therapeutic concentrations in the kidney. Antibiotics that don't achieve adequate renal tissue levels, such as nitrofurantoin, fosfomycin and pivmecilinam, are avoided.
- Urine should be sent for culture to confirm susceptibility of the bacteria and inform treatment choice.
- The committee reviewed the available evidence comparing different antibiotics in adults and children and agreed that it was limited by its setting (most studies in adults were undertaken in a hospital, and in children the setting of the studies was not reported). The studies included various different antibiotics, which may not reflect those chosen in UK practice. The committee discussed the evidence for a benefit of the intravenous third-generation cephalosporins, ceftolozane/tazabactam or ceftazidime, over an intravenous quinolone, but this was mainly limited to a benefit for composite cure (which included clinical cure, microbiological eradication and microbiological cure) and the absolute benefits were small.
- The committee agreed, based on experience, that several oral and intravenous antibiotics should be available for people with acute pyelonephritis. This enables antibiotics to be selected based on the severity of illness, antibiotic susceptibilities from culture results when available, local resistance patterns, risk of resistant bacteria, the setting, and known patient factors (such as whether the person has a [higher risk urinary tract infection](#)). In line with antimicrobial stewardship, narrower spectrum antibiotics should be used wherever possible. However, antibiotics that don't achieve adequate renal tissue levels, such as nitrofurantoin, fosfomycin and pivmecilinam, are avoided.

- The committee agreed that any recent previous urine culture and susceptibility results, and antibiotic prescribing, should be reviewed before choosing an antibiotic.
- Based on experience, the committee agreed that when results of urine cultures are available, if the results suggest the antibiotic given is not susceptible, the antibiotic should be changed regardless of whether symptoms are improving or not.

Non-pregnant women and men with acute pyelonephritis

- Based on evidence, their experience and resistance data, the committee agreed to recommend a choice of first-line **oral antibiotics**, at usual doses for acute pyelonephritis. These are:
 - **co-amoxiclav** (a penicillin with a beta-lactamase inhibitor): which is widely used because common causative pathogens in acute pyelonephritis are susceptible, despite there being less evidence for its use.
 - **ciprofloxacin** or **levofloxacin** (quinolones): which would be suitable alternatives, particularly for those who have had previous penicillin treatment or as an alternative for penicillin allergy or if penicillins are not tolerated, because common causative pathogens in acute pyelonephritis are susceptible to quinolones.
 - **trimethoprim**: which is only suitable if culture results are available and bacteria are susceptible, because resistance rates are high.
- The committee noted that use of broad-spectrum antibiotics, such as co-amoxiclav, cephalosporins or quinolones, can create a selective advantage for bacteria resistant to these second-line broad-spectrum agents, allowing such strains to proliferate and spread. And, by disrupting normal flora, broad-spectrum antibiotics can leave people susceptible to harmful bacteria such as *Clostridium difficile* infection in community settings. However, these antibiotics are appropriate for the empirical treatment of acute pyelonephritis, where coverage of more resistant strains of common bacterial pathogens is required.
- Based on evidence, their experience and resistance data, the committee

agreed to recommend a choice of first-line **intravenous antibiotics**, at usual doses for acute pyelonephritis, for people who are unable to take oral antibiotics due to nausea and vomiting, or are more severely unwell.

These are:

- **co-amoxiclav** or **ciprofloxacin**; which can be given intravenously.
- **ceftriaxone** (a third generation cephalosporin): which would be a suitable alternative to co-amoxiclav or ciprofloxacin.
- **gentamicin** or **amikacin** (aminoglycosides): which may be appropriate for some people with acute pyelonephritis, particularly those with severe infection or sepsis, but that efforts should be made to identify the causal bacteria and use reviewed at 48 hours. Gentamicin is the preferred aminoglycoside in the UK but shortages may result in the use of amikacin.
- The committee agreed, based on experience, that it may be necessary to combine antibiotics in the care of people with suspected sepsis. This should be done according to local policy or on the advice of a microbiologist.

Pregnant women with acute pyelonephritis

- Based on their experience and resistance data, the committee agreed to recommend **cefalexin** (a first generation cephalosporin) as the first-choice oral antibiotic for pregnant women who don't require intravenous antibiotics, and **cefuroxime** (a second generation cephalosporin) as the first choice intravenous antibiotic.

Children and young people with acute pyelonephritis

- The committee was aware that the [NICE guideline on urinary tract infection in under 16s: diagnosis and management](#) makes recommendations on diagnosing acute pyelonephritis, offering antibiotic treatment and considering referral to a paediatric specialist.
- Based on the NICE guideline, evidence, their experience and resistance data, the committee agreed to recommend **co-amoxiclav** or **cefalexin**, at usual doses for acute pyelonephritis, as first-choice **oral antibiotics**.

- Based on the NICE guideline, evidence, their experience and resistance data, the committee agreed to recommend a choice of first-line **intravenous antibiotics**, at usual doses, for children and young people who are unable to take oral antibiotics due to nausea and vomiting, or are more severely unwell. These are:
 - **co-amoxiclav**; which can be given intravenously.
 - **cefotaxime** or **ceftriaxone** (third generation cephalosporins): which would be suitable alternatives to co-amoxiclav.
 - **gentamicin** or **amikacin** (aminoglycosides): which may be appropriate for some children and young people with acute pyelonephritis, particularly those with severe infection or sepsis, but that efforts should be made to identify the causal bacteria and use reviewed at 48 hours.
- The committee agreed, based on experience, that it may be necessary to combine antibiotics in the care of children and young people with suspected sepsis. This should be done according to local policy or on the advice of a microbiologist.

Antibiotic course length

- The evidence for antibiotic course length in the treatment of acute pyelonephritis in adults comes from 2 systematic reviews ([Eliakim-Raz et al. 2013](#) and [Kyriakidou et al. 2008](#)) and 1 RCT ([Ren et al. 2017](#)). No significant differences were found for clinical, microbiological or safety and tolerability outcomes between short courses and longer courses of antibiotics (7 days or less compared with 10 days to 6 weeks in 1 systematic review, and 7 to 14 days compared with 14 to 42 days in the other systematic review [very low to moderate quality evidence]). There were no significant differences between a short course (5 days) of intravenous levofloxacin (750 mg once daily) and a longer course (7 to 14 days) of intravenous and then oral levofloxacin (500 mg once daily) (moderate quality evidence).
- Evidence from 1 systematic review in children with acute pyelonephritis (Strohmeier et al. 2014) found some significant differences in clinical

effectiveness between different antibiotic course lengths. However, this was limited to 1 RCT of 10 days compared with 42 days of oral sulphafurazole (moderate quality evidence), with other studies in the review finding no differences in outcomes (very low quality evidence). Safety and tolerability outcomes were not reported.

Committee discussions on antibiotic course length

- The committee agreed that the shortest course that is likely to be effective should be prescribed to reduce the risk of antimicrobial resistance and minimise the risk of adverse effects.
- Based on evidence, the committee agreed that a short course of antibiotics was as effective as a long course of antibiotics for acute pyelonephritis, but the definition of short and long course differed depending on the clinical trial definition and the antibiotic used.
- In line with the NICE guideline on [antimicrobial stewardship](#) and [Start smart – then focus](#), the committee agreed that the use of intravenous antibiotics should be reviewed by 48 hours (taking into account the person's response to treatment and susceptibility results from urine culture) and switched to oral treatment where possible.

Non-pregnant women and men with acute pyelonephritis

- Based on evidence, their experience and resistance data, the committee agreed that, for oral treatment, a 7-day course of co-amoxiclav, ciprofloxacin or levofloxacin, or a 14-day course of trimethoprim was sufficient to treat acute pyelonephritis in non-pregnant women and men. For intravenous treatment, antibiotics should be reviewed by 48 hours and stepped down to oral antibiotics where possible, for a total of 7 days.

Pregnant women with acute pyelonephritis

- Based on evidence, their experience and resistance data, the committee agreed that, for oral treatment, a 7-day course of cefalexin was sufficient to treat acute pyelonephritis in pregnant women. For intravenous treatment, antibiotics should be reviewed by 48 hours and stepped down

to oral antibiotics where possible, for a total of 7 days.

Children and young people with acute pyelonephritis

- The committee was aware that the NICE guideline on [urinary tract infection in under 16s: diagnosis and management](#) makes recommendations on antibiotic treatment for children and young people under 16 with acute pyelonephritis, which it supported and provided more detail on.
- Based on the NICE guideline, evidence, their experience and resistance data, the committee agreed that a 7- to 10-day course of oral antibiotics (co-amoxiclav or cefalexin) was required to treat acute pyelonephritis in children and young people. For intravenous treatment, antibiotics should be reviewed by 48 hours and stepped down to oral antibiotics where possible, for a total of 10 days.

Antibiotic dose frequency

- No systematic reviews or RCTs that compared the frequency of antibiotic dosing in adults were identified that met the inclusion criteria.
- Evidence from 1 systematic review in children with acute pyelonephritis (Strohmeier et al. 2014) found no significant difference in the clinical effectiveness of aminoglycosides with once daily administration compared with 8-hourly administration (moderate quality evidence). There were no significant differences in the number of children with hearing impairment or kidney dysfunction (very low quality evidence).

Antibiotic route of administration

- The evidence for route of antibiotic administration in acute pyelonephritis is based on 1 systematic review of 15 RCTs in adults and children ([Pohl 2007](#)). This review addressed different modes of administration of antibiotics which cover:
 - sequential intravenous then oral treatment compared with intravenous or intramuscular treatment
 - sequential intravenous then oral treatment compared with oral treatment
 - oral treatment compared with intravenous or intramuscular treatment

- single dose intravenous or intramuscular treatment then oral treatment compared with sequential intravenous then oral treatment.
- Overall, this review found that oral antibiotics were as effective as other routes of administration in treating symptomatic severe UTI (including pyelonephritis) in both adults and children. Intravenous or intramuscular antibiotics were significantly better for bacteriological cure than oral antibiotics at the end of treatment, but this is based on 1 small RCT (NNT 4 [range 3 to 15]; low quality evidence).
- There were no significant differences in adverse effects between different routes of administration of antibiotics (very low quality evidence).
- Further evidence is available from 1 systematic review in children with acute pyelonephritis (Strohmeier et al. 2014) which compared different routes of administration which cover:
 - oral treatment compared with sequential intravenous then oral treatment
 - sequential intravenous then oral treatment (short course of 3 to 4 days) compared with intravenous treatment (longer course of 7 to 14 days)
 - single dose intramuscular then oral treatment compared with oral treatment
 - oral treatment compared with rectal treatment
- Overall, this review found no significant differences in the clinical effectiveness of oral antibiotics (cephalosporins or co-amoxiclav) in children with acute pyelonephritis compared with other routes of administration (very low to moderate quality evidence).
- Safety and tolerability outcomes were poorly reported in the RCTs included in Strohmeier et al (2014), but there did not appear to be any significant differences between different routes of administration of antibiotics (very low quality evidence).

Committee discussions on antibiotic route of administration

- Based on evidence, the committee agreed that, overall, oral antibiotics were as effective as other routes of administration for treating acute pyelonephritis in adults and children.
- The committee agreed, based on evidence and experience, that oral antibiotics should be given first-line where people have the ability to take oral medicines and the severity of their condition does not require intravenous antibiotics.
- The committee agreed, based on evidence and experience, that intravenous antibiotics can be used for people who are unable to take oral antibiotics due to nausea and vomiting, or are more severely unwell, in line with the Department of Health guidance – Start Smart Then Focus.

See the full evidence review for more information.

Other considerations

Medicines adherence

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

Resource implications

- One small RCT ([Moramezi et al. 2008](#)) in pregnant women with acute pyelonephritis found no significant difference in length of hospital stay in women taking a cephalosporin compared with ampicillin plus gentamicin (p=0.22; very low quality evidence).
- One RCT ([Talan et al. 2000](#)) which compared ciprofloxacin with co-trimoxazole in adult women with acute pyelonephritis found that resource use (hospital stay, visits and telephone contacts, laboratory tests and prescription costs) was higher in the co-trimoxazole group (no analysis reported). The only exception was for radiological procedures which was

slightly higher in the ciprofloxacin group (no analysis reported). One systematic review ([Eliakim-Raz et al. 2013](#)) which compared antibiotic course lengths in adults with acute pyelonephritis included the Talan et al. (2000) study and noted a shorter duration of hospital stay with a short course of antibiotics (7 days or less) compared with a longer course (10 days to 6 weeks).

- One RCT in the systematic review by [Strohmeier et al \(2014\)](#) in children with acute pyelonephritis found that giving sequential intravenous then oral antibiotics reduced the duration of hospital stay compared with a longer duration of intravenous antibiotics (4.9 days compared with 9.8 days).
- Recommended antibiotics (trimethoprim, co-amoxiclav, cephalosporins, quinolones and aminoglycosides) are available as generic formulations, see [Drug Tariff](#) for costs.