





Prostatitis (acute): antimicrobial prescribing

NICE guideline

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Your responsibility

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

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 impact of implementing NICE recommendations</u> wherever possible.

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Overview

This guideline sets out an antimicrobial prescribing strategy for acute prostatitis. It aims to optimise antibiotic use and reduce antibiotic resistance.

See a <u>2-page visual summary</u> of the recommendations, including a table to support prescribing decisions.

NICE has also produced a guideline on <u>antimicrobial stewardship</u>: systems and processes for effective antimicrobial medicine use.

Who is it for?

- Health professionals
- People with acute prostatitis, their families and carers

Recommendations

1.1 Managing acute prostatitis

- 1.1.1 Be aware that acute prostatitis:
 - is a bacterial infection of the prostate needing treatment with antibiotics
 - is usually caused by bacteria entering the prostate from the urinary tract
 - can occur spontaneously or after medical procedures such as prostate biopsy
 - can last several weeks
 - can cause complications such as acute urinary retention and prostatic abscess.

Treatment

- 1.1.2 Offer an antibiotic (see the recommendations on <u>choice of antibiotic</u>) to people with acute prostatitis. Take account of:
 - the severity of symptoms
 - the risk of developing complications or having treatment failure, particularly after medical procedures such as prostate biopsy
 - previous urine culture and susceptibility results
 - previous antibiotic use, which may have led to resistant bacteria.
- 1.1.3 Obtain a midstream urine sample before antibiotics are taken and send for culture and susceptibility testing.
- 1.1.4 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 a narrow spectrum antibiotic wherever possible.

Advice when an antibiotic prescription is given

- 1.1.5 When an antibiotic is given, give advice about:
 - the usual course of acute prostatitis (several weeks)
 - possible adverse effects of the antibiotic, particularly diarrhoea and nausea
 - seeking medical help if:
 - symptoms worsen at any time, or
 - symptoms do not start to improve within 48 hours of taking the antibiotic, or
 - the person becomes systemically very unwell.

Reassessment

- 1.1.6 Reassess if symptoms worsen at any time, taking account of:
 - other possible diagnoses
 - any symptoms or signs suggesting a more serious illness or condition, such as acute urinary retention, prostatic abscess or sepsis
 - previous antibiotic use, which may have led to resistant bacteria.

Referral

- 1.1.7 Refer people with acute prostatitis to hospital if:
 - they have any symptoms or signs suggesting a more serious illness or condition (for example sepsis, acute urinary retention or prostatic abscess), or
 - their symptoms are not improving 48 hours after starting the antibiotic.

See the evidence and committee discussion on antibiotics.

1.2 Self-care

1.2.1 Advise people with acute prostatitis about using paracetamol (with or without a low-dose weak opioid, such as codeine) for pain, or ibuprofen if this is preferred and suitable.

1.2.2 Advise people with acute prostatitis about drinking enough fluids to avoid dehydration.

See the evidence and committee discussion on self-care.

1.3 Choice of antibiotic

- 1.3.1 When prescribing an antibiotic for acute prostatitis, take account of <u>local</u> antimicrobial resistance data and follow table 1 for adults aged 18 years and over.
- 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.
- 1.3.4 Review antibiotic treatment after 14 days and either stop the antibiotic or continue for a further 14 days if needed, based on an assessment of the person's history, symptoms, clinical examination, urine and blood tests.

Table 1 Antibiotics for adults aged 18 years and over

| Antibiotic ¹ | Dosage and course length | | | | | | | |
|---|--|--|--|--|--|--|--|--|
| First-choice oral antibiotic (guided by susceptibilities when available) ² | | | | | | | | |
| Ciprofloxacin ³ | 500 mg twice a day for 14 days then review ⁴ | | | | | | | |
| Ofloxacin ³ | 200 mg twice a day for 14 days then review ⁴ | | | | | | | |
| Alternative first-choice oral antibiotic for adults unable to take a fluoroquinolone (guided by susceptibilities when available) ² | | | | | | | | |
| Trimethoprim | 200 mg twice a day for 14 days then review ⁴ | | | | | | | |
| Second-choice oral antibiotic (after discussion with specialist) | | | | | | | | |
| Levofloxacin ³ | ocin ³ 500 mg once a day for 14 days then review ⁴ | | | | | | | |
| Co-trimoxazole ⁵ 960 mg twice day for 14 days then review ⁴ | | | | | | | | |

| First-choice intravenous antibiotics (if unable to take oral antibiotics or severely unwell; guided by susceptibilities when available). Antibiotics may be combined if sepsis a concern ^{2,6} | | | | | | | |
|---|---|--|--|--|--|--|--|
| Ciprofloxacin ³ | 400 mg twice or three times a day | | | | | | |
| Levofloxacin ³ | 500 mg once a day | | | | | | |
| Cefuroxime | 1.5 g three or four times a day | | | | | | |
| Ceftriaxone | 2 g once a day | | | | | | |
| Gentamicin | Initially 5 to 7 mg/kg once a day, subsequent doses adjusted according to serum gentamicin concentration ⁷ | | | | | | |
| Amikacin | Initially 15 mg/kg once a day (maximum per dose 1.5 g once a day), subsequent doses adjusted according to serum amikacin concentration (maximum 15 g per course) ⁷ | | | | | | |

Second-choice intravenous antibiotic

Consult local microbiologist

See the evidence and committee discussion on choice of antibiotic.

¹See <u>BNF</u> for appropriate use and dosing in specific populations, for example, hepatic impairment and renal impairment, and administering intravenous antibiotics.

²Check any previous urine culture and susceptibility results and antibiotic prescribing and choose antibiotics accordingly.

³The European Medicines Agency's Pharmacovigilance Risk Assessment Committee has recommended restricting the use of fluoroquinolone antibiotics following a review of disabling and potentially long-lasting side effects mainly involving muscles, tendons, bones and the nervous system (press release October 2018), but they are appropriate in acute prostatitis which is a severe infection.

⁴Review treatment after 14 days and either stop the antibiotic or continue for a further 14 days if needed based on clinical assessment.

⁵Co-trimoxazole should only be considered when there is bacteriological evidence of sensitivity and good reasons to prefer this combination to a single antibiotic (BNF, August 2018).

⁶Review intravenous antibiotics by 48 hours and consider stepping down to oral antibiotics where possible for a total of 14 days then review.

⁷Therapeutic drug monitoring and assessment of renal function is required (BNF, August 2018).

Summary of the evidence

Self-care

• No systematic reviews, randomised controlled trials (RCTs) or observational studies of the efficacy of non-antimicrobial treatments for acute prostatitis were identified.

Committee discussion on self-care

- Based on experience, the committee agreed that it was reasonable to advise adults with acute prostatitis about paracetamol (with or without a low-dose weak opioid, such as codeine) for self-care management of pain. These medicines have a well-established efficacy and safety profile for managing pain.
- If preferred and suitable, ibuprofen could be considered. However, the safety profile of nonsteroidal anti-inflammatory drugs (NSAIDs) and drug interactions (potential increased risk of seizures with fluoroquinolones) should be taken into account when selecting pain relief.
- Based on experience that dehydration is often cited as a cause of urinary tract infections, the committee agreed that people should be advised about drinking enough fluids to avoid dehydration.

Antibiotics

- Acute prostatitis is a bacterial infection needing prompt treatment with antibiotics.
- Gram-negative bacteria are the most common causative pathogens in acute prostatitis, most commonly *Escherichia coli*, *Proteus* species, *Klebsiella* species and *Pseudomonas* species.
- Complications of acute prostatitis include acute urinary retention secondary to prostatic oedema, chronic prostatitis, prostatic abscess, bacteraemia, epididymitis and pyelonephritis.

Efficacy of antibiotics

• No systematic reviews, RCTs or observational studies of the efficacy of antibiotics for treating acute prostatitis were identified.

Safety of antibiotics

• Fluoroquinolones can interact with NSAIDs, potentially increasing the risk of seizures (BNF,

- <u>August 2018</u>). Tendon damage (including rupture) has been reported rarely in people receiving fluoroquinolones (BNF, August 2018), and the European Medicines Agency's
 Pharmacovigilance Risk Assessment Committee (<u>press release October 2018</u>) 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 remain appropriate in acute prostatitis, which is a severe infection.
- Antibiotic-associated diarrhoea occurs in 2% to 25% of people taking antibiotics, depending on the antibiotic used (NICE clinical knowledge summary on diarrhoea antibiotic associated).
- About 10% of the general population claim to have a penicillin allergy; this has often been because of a skin rash that occurred during a course of penicillin in childhood. Fewer than 10% of people who think they are allergic to penicillin are truly allergic. See the NICE guideline on drug allergy for more information.
- People with a history of immediate hypersensitivity to penicillins may also react to cephalosporins and other beta-lactam antibiotics (BNF, August 2018).
- Aminoglycoside doses are based on weight and renal function and whenever possible treatment should not exceed 7 days (BNF, August 2018).
- There are restrictions on the use of co-trimoxazole in the UK. It should only be used in urinary tract infections where there is bacteriological evidence of sensitivity and good reasons to prefer this antibiotic (BNF, August 2018).
- See the <u>summaries of product characteristics</u> and <u>BNF</u> for information on contraindications, cautions and adverse effects of individual medicines.

Committee discussion on antibiotics

- The committee agreed that acute prostatitis is a bacterial infection needing prompt treatment with antibiotics, but no evidence was identified to support this.
- The committee was aware of several guidelines, which reflect current practice, that make recommendations based on expert consensus and overviews of the literature on pharmacokinetics and antimicrobial resistance patterns.
- Based on experience, the committee agreed that adults with acute prostatitis should be offered an antibiotic. Urine should be sent for culture to confirm susceptibility of the bacteria and inform treatment choice.
- The committee agreed that if the results of urine culture suggest the bacteria are resistant
 to the antibiotic given, adults with acute prostatitis should be contacted and the antibiotic
 should be changed. In line with good antimicrobial stewardship, narrow-spectrum
 antibiotics should be used wherever possible, and antibiotics switched from intravenous to
 oral where applicable.
- The committee agreed that if symptoms do not start to improve within 48 hours of taking an antibiotic, people should be referred to hospital because of concerns around complications, such as acute urinary retention or prostatic abscess, and treatment failure because of resistant bacteria.

Choice of antibiotic

- Many antibiotics penetrate the prostate gland poorly, but fluoroquinolones reach therapeutic levels in the prostate. Where fluoroquinolone resistance is a concern, other antibiotics that can reach therapeutic prostate levels include third-generation cephalosporins (such as ceftriaxone), carbapenems (such as imipenem or ertapenem), some aminoglycosides, aztreonam, piperacillin, minocycline, doxycycline, erythromycin, clindamycin and trimethoprim (Lipsky et al. 2010). In acute prostatitis, where there is intense inflammation of the prostate gland, antibiotic penetration can be better than in chronic prostatitis (National guidelines for the management of prostatitis, BASHH, 2001).
- Several guidelines make recommendations on antibiotic choice based on expert consensus and overviews of the literature on pharmacokinetics and antimicrobial resistance patterns. These include:
 - European Association of Urology guidelines on urological infections (2018)

| • – | RCGP | /RASH | H Sexually | v transmitted | infections | s in primar | y care guidelines | (2013) |
|-----|--------|--------|-------------|---------------|------------|-----------------|-------------------|---------------------------|
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- BASHH national guidelines for the management of prostatitis (2001).

Committee discussion on choice of antibiotic

- No evidence was identified to guide the choice of antibiotics for treating acute prostatitis. The committee was aware of several guidelines, which reflect current practice, that make recommendations based on expert consensus and overviews of the literature on pharmacokinetics and antimicrobial resistance patterns.
- Based on experience, the committee agreed that treating acute prostatitis requires high doses of fluoroquinolones, second- or third-generation cephalosporins or broad-spectrum penicillins (possibly combined with an aminoglycoside), with intravenous or oral use based on the severity of symptoms and the ability to take oral medicines. These antibiotics reach therapeutic levels in the prostate, and are in line with current guidelines and practice.
- Nationally for England, resistance of *E. coli* (the main causative organism of acute prostatitis) in laboratory processed urine specimens to the following antibiotics is:
 - ciprofloxacin: 10.6% (varies by area from 7.8% to 13.7%)
 - trimethoprim: 30.3% (varies by area from 27.1% to 33.4%)
 (Public Health England. Antimicrobial resistance quarterly surveillance: March 2018).
- The committee also discussed that prescribers should be aware of their local antimicrobial prescribing data, because resistance rates do vary by area.
- Based on experience and resistance data, the committee agreed that the choice of first- and second-line oral antibiotics for managing acute prostatitis are:
 - First-choice: ciprofloxacin or ofloxacin (fluoroquinolones), or trimethoprim (for adults unable to take a fluoroquinolone). Fluoroquinolones are more effective against a wider range of urinary pathogens than trimethoprim. But for adults unable to take a fluoroquinolone, trimethoprim is recommended. Trimethoprim generally has a lower risk of resistance in men, and can reach therapeutic prostate levels.
 - Second-choice: levofloxacin (a fluoroquinolone) or co-trimoxazole
- The committee agreed that second-choice oral antibiotics should be reserved for use after discussion with a specialist. This is to preserve the use of the broader spectrum fluoroquinolone, levofloxacin, for people with a more severe infection, and because of restrictions on the use of co-trimoxazole in the UK.

- The committee was aware of the European Medicines Agency's Pharmacovigilance Risk Assessment Committee recommendation to restrict the use of fluoroquinolone antibiotics following a review of disabling and potentially long-lasting side effects mainly involving muscles, tendons and bones and the nervous system. However, they discussed that fluoroquinolone antibiotics are the mainstay of treatment in acute prostatitis, which is a severe infection. The committee was keen to point out, however, that fluoroquinolone safety concerns should be taken into account on an individual patient basis.
- The committee agreed that the choice of intravenous antibiotics for managing acute prostatitis in people who are severely unwell or unable to take oral antibiotics (with combined use if sepsis is a concern) are:
 - ciprofloxacin or levofloxacin (fluoroquinolones)
 - cefuroxime or ceftriaxone (second- or third-generation cephalosporins)
 - gentamicin or amikacin (aminoglycosides).
- This choice allows intravenous antibiotics to be selected based on the severity of illness and likely pathogens, antibiotic susceptibilities from culture results when available, and local resistance data.
- The committee noted that use of broad-spectrum antibiotics, such as fluoroquinolones or later-generation cephalosporins, 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* in community settings. However, these antibiotics are appropriate for the empirical treatment of acute prostatitis, where coverage of more resistant strains of common bacterial pathogens is required.

Antibiotic course length

- Several guidelines make recommendations on antibiotic course length based on expert consensus and overviews of the literature on pharmacokinetics and antimicrobial resistance patterns. These include:
 - European Association of Urology guidelines on urological infections (2018)
 - RCGP/BASHH Sexually transmitted infections in primary care guidelines (2013)

- BASHH national guidelines for the management of prostatitis (2001).
- In line with Department of Health and Social Care guidance (<u>Start smart then focus</u>), the NICE guideline on <u>antimicrobial stewardship</u> recommends considering a review of intravenous antibiotic prescriptions at 48 to 72 hours, documenting response to treatment and any available culture and susceptibility results to determine if the antibiotic should be continued or switched to a narrower spectrum or an oral antibiotic.

Committee discussion on antibiotic course length

- No evidence was identified to guide antibiotic course length for treating acute prostatitis.
 The committee was aware of several guidelines that make recommendations based on expert consensus and overviews of the literature on pharmacokinetics and antimicrobial resistance patterns.
- Based on experience, the committee agreed that treating acute prostatitis requires oral antibiotics for between 2 and 4 weeks, with initial intravenous antibiotics if adults are unable to take oral antibiotics or are severely unwell. This is in line with current guidelines and practice.
- However, in line with good antimicrobial stewardship, 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. First-line antibiotics for acute prostatitis are fluoroquinolones, which are broad-spectrum antibiotics. These antibiotics, in particular, should be used for the shortest effective time because they can create a selective advantage for bacteria resistant to these 'last-line' broad-spectrum agents, and can leave people susceptible to *Clostridium difficile*.
- 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.
- The committee agreed that a minimum of a 14-day course of all the recommended antibiotics was required for acute prostatitis. At 14 days, treatment should be reviewed, and either stopped or continued for a further 14 days as needed based on clinical assessment. From experience, the committee discussed that whether to continue treatment or not would be based on the person's history or risk of developing chronic prostatitis, their current symptoms and any recent examination, urine and blood test results. Continued symptoms, such as fever or lower urinary tract symptoms (dysuria, frequency, urgency, or acute urinary retention) require ongoing treatment.

Antibiotic prophylaxis for preventing infective complications, including acute prostatitis, after biopsy

• One double blind RCT from Iran (<u>Dadashpour et al. 2016</u>) and 4 observational studies from Taiwan, Turkey or Korea (<u>Lee et al. 2015</u>, <u>Chiang et al. 2007</u>, <u>Ryu et al. 2016</u> and <u>Bulut et al. 2015</u>) compared the effectiveness of various short-term antibiotic regimens in preventing complications, including acute prostatitis, after prostate biopsy. All the observational studies were retrospective analyses of medical records, often with non-concurrent controls. The prophylactic antibiotics varied, but most studies used a fluoroquinolone. The definition of post-biopsy complications, including acute prostatitis, varied between clinical symptoms (fever more than 38°C or more than 39°C, chills, dysuria, frequent urination and pelvic pain), abnormal digital rectal examination or urinalysis.

Committee discussion on preventing acute prostatitis and other complications after prostate biopsy

- The committee reviewed the available evidence and agreed that it was limited by its design (mostly observational studies) and its relevance to UK practice (studies were undertaken in Iran, Taiwan, Turkey and Korea where the choice of antibiotics may be very different).
- The committee agreed that the limitations with the evidence base, and the wide range of antibiotics included at varying dosage regimens, makes interpretation of study findings difficult.
- The committee agreed that the available evidence on antibiotic prophylaxis was insufficient to make recommendations and local microbiologists should be consulted.

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

• Recommended antibiotics are all available as generic formulations, see <u>Drug Tariff</u> for costs.

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Accreditation

