Acute Bacterial Prostatitis

CHI Formulary Indication Review

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INDICATION UPDATE

ADDENDUM – August 2023

To the CHI Original Acute Bacterial Prostatitis Clinical Guidance- Issued February 2020

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Related Documents

Related SOPs

- IDF-FR-P-02-01-IndicationsReview&IDFUpdates
- IDF-FR-P-05-01-UpdatedIndicationReview&IDFUpdates

Related WI:

- IDF-FR-WI-01-01SearchMethodologyGuideForNewIndications

Abbreviations

AAFP	American Academy of Family Physicians
AAUS	Asian Association of UTI & STI
ABP	Acute Bacterial Prostatitis
BLI	Beta-Lactamase Inhibitor
BP	Bacterial Prostatitis
CHI	Council of Health Insurance
CPB	Chronic Bacterial Prostatitis
CPG	Clinical Practice Guidelines
CNS	Central Nervous System
cUTI	Complicated Urinary Tract Infections
E. coli	Escherichia coli
EAU	European Association of Urology
EMA	European Medicines Agency
ESBL	Extended Spectrum Beta-Lactamase
FDA	Food and Drug Administration
FQ	Fluoroquinolones
GR	Grades of Guideline Recommendations
KSA	Kingdom of Saudi Arabia
IDF	CHI Drug Formulary
IV	Intravenous
LE	Levels of Evidence
NICE	National Institute for Health and Care Excellence
PA	Prior Authorization
SFDA	Saudi Food and Drug Authority
ST	Step Therapy
TRPB	Transrectal Prostate Biopsy
TRUS	Transrectal Ultrasound
UTI	Urinary Tract Infection

Executive Summary

Bacterial prostatitis (BP) is a bacterial infection of the prostate gland. It can be acute bacterial prostatitis (ABP) or chronic bacterial prostatitis (CBP) in nature. This report will focus solely on acute bacterial prostatitis[1].

Patients with ABP present with fever, chills, and urinary symptoms. If not treated appropriately, ABP can result in significant morbidity and complications such as prostatic abscess or sepsis[1].

ABP is most commonly caused by the *Enterobacteriaceae* family (mainly *E. coli*). Gram-positive organisms such as *Enterococcus species* and *Staphylococcus species*, as well as sexually transmitted organisms such as *Neisseria gonorrhoeae, Chlamydia trachomatis,* and *Ureaplasma urealyticum*, can be associated with ABP. It is worth noting that manipulations of the prostate, such as transrectal or transurethral prostate biopsies, cystoscopy, and catheterization, can increase the risk of infections caused by pseudomonas, mixed organisms, staphylococci, and can also lead to treatment failure[1].

In general, urinary tract infections (UTIs) continue to pose a significant challenge for the healthcare system in the Kingdom of Saudi Arabia (KSA). They constitute 10% of all infections within the country and rank as the second most frequent cause of emergency department admissions. Approximately 4% of patients with UTIs require hospitalization for additional medical care. Additionally, readmission rates are a concern, with around 10% of patients being readmitted within one week of their initial discharge, often due to ineffective treatment. Similar problems are faced around the world, as has been reported by several studies[2].

Antimicrobial therapy remains the mainstay of treatment, along with supportive management.

CHI issued Acute Bacterial Prostatitis clinical guidance after thorough review of renowned international and national clinical guidelines in February 2020. Updating clinical practice guidelines (CPGs) is a crucial process for maintaining the validity of recommendations.

This report functions as an addendum to the prior CHI ABP clinical guidance and seeks to offer guidance for the effective management of ABP. It provides an **update on the ABP Guidelines** for CHI Formulary with the ultimate objective of updating the IDF (CHI Drug Formulary) while addressing **the most updated best available clinical and economic evidence related to drug therapies.**

Main triggers for the update are summarized, being **the issuance of updated versions of previously reviewed guidelines** namely the NICE guidelines for antimicrobial prescribing for urinary tract infections published in June (**2019**), **the missing recommendations** from the American Academy Family Physicians (AAFP) guidelines for Acute Bacterial Prostatitis: Diagnosis and Management (**2016**). Moreover, **new guidelines are added to the report** such as the Asian Association of UTI & STI (AAUS) guideline for acute bacterial prostatitis (**2021**) and the European Association of Urology (EAU) guidelines on urological infections (**2023**).

After carefully examining clinical guidelines and reviewing the SFDA drug list, it is important to note that there have been **no withdrawals or newly approved drugs** for the treatment of ABP. Additionally, there have been **updates** regarding certain previously mentioned drugs in terms of drug information and prescribing edits since February 2020.

All recommendations are well supported by reference guidelines, Grade of Recommendation (GoR), Level of Evidence (LoE) and Strength of Agreement (SoA) in all tables reflecting specific drug classes' role in the ABP therapeutic management.

Below is a table summarizing the major changes based on the different ABP guidelines used to issue this report:

Table 1. General Recommendations for the Management of Acute Bacterial Prostatitis

Management of Acute Bacterial Prostatitis		
General Recommendations	**Level of Evidence/Grade of Recommendation**	**Reference**
First-choice oral antibiotics (guided by susceptibilities when available) are ciprofloxacin or ofloxacin. Safety of fluoroquinolones (FQs) should be taken into consideration. Alternative first-choice oral antibiotics if a FQ is not appropriate (guided by susceptibilities when available) is Trimethoprim. Specialist advice should be sought.	Not graded	NICE Guidelines 2018[3]

Second-choice oral antibiotics (after discussion with specialist) are levofloxacin or co-trimoxazole.	Not graded	NICE Guidelines 2018[3]
The first-line options for intravenous (IV) treatment are ciprofloxacin, levofloxacin, cefuroxime, ceftriaxone, gentamicin, and amikacin, which should only be used if the patient is unable to take oral antibiotics or is severely unwell (if unable to take oral antibiotics or severely unwell; guided by susceptibilities when available). Antibiotics may be combined if sepsis a concern.	Not graded	NICE Guidelines 2018[3]
For second-choice intravenous antibiotics, it is recommended to consult local microbiologist.	Not graded	NICE Guidelines 2018[3]
If there is a risk for sexually transmitted disease, a single dose of ceftriaxone or a single dose of cefixime; followed by doxycycline for 10 days are the recommended regimens.	Not graded	AAFP Guidelines 2016[4]
If the patient is severely ill with no resistant risk factors, then the first choice is piperacillin/tazobactam plus aminoglycosides **or** cefotaxime plus aminoglycosides **or** ceftazidime plus aminoglycosides.	Not graded	AAFP Guidelines 2016[4]
If transrectal manipulation, FQ resistance, and extended spectrum beta-lactamase–producing *Escherichia coli*, first choice is piperacillin/tazobactam plus aminoglycosides	Not graded	AAFP Guidelines 2016[4]
If transurethral manipulation—*Pseudomonas* species, or FQ exposure—fluoroquinolone resistance, first choice is piperacillin/tazobactam, **or** ceftazidime, **or** cefepime	Not graded	AAFP Guidelines 2016[4]

In patients with a complicated UTI (including ABP) with systemic symptoms, empirical treatment should cover ESBL if there is an increased likelihood of ESBL infection based on prevalence in the community, earlier collected cultures and prior antimicrobial exposure of the patient.	LE: 2	EAU Guidelines 2023[5]
Third-generation cephalosporins, a broad-spectrum beta-lactam/beta-lactamase inhibitor (BLI), or carbapenems are recommended for patients with ABP requiring hospitalization or if the resistance of the causative bacteria to fluoroquinolone is considered.	LE: 4	AAUS Guidelines 2021[6]
In the group of patients with prior manipulation in which pathogens other than *E. coli* constitute a substantial number of isolates, a combination of a cephalosporin and amikacin should be recommended for empirical therapy.	GR: B	AAUS Guidelines 2021[6]
Supportive measures include intravenous hydration and catheter drainage if the patient cannot void.	GR: B	AAUS Guidelines 2021[6]
Although no consensus currently exists on optimal treatment duration, some guidelines (AAUS 2021) recommend that the oral antibiotic therapy should be continued at least for 2–4 weeks. While other references (Lexicomp 2023) recommend 4-6 weeks as a duration of therapy. Hence, a range of 2-6 weeks duration of treatment could be prescribed based on the patient's response and the disease's severity.	AAUS Guidelines: LE: 4 Lexicomp: Not graded	AAUS Guidelines 2021[6] Lexicomp 2023[7]

At the end of the report, a **key recommendation synthesis section** is added highlighting the latest updates in **Acute Bacterial Prostatitis clinical and therapeutic management.**

Section 1.0 Summary of Reviewed Clinical Guidelines & Evidence

This section is divided into two parts: the first includes recommendations from **updated versions of guidelines** mentioned in the previous CHI ABP report, while the second includes **newly added guidelines** that have helped generate this report.

1.1. Revised Guidelines

This section contains the **updated versions** of the guidelines mentioned in the March 2020 CHI ABP Report and the corresponding recommendations.

Table 2. Guidelines Requiring Revision

Guidelines Requiring Revision	
Old Versions	**Updated versions**
1.1.1. Prostatitis (acute): antimicrobial prescribing **NICE guideline** Published date: **October 2018**	N/A*
1.1.2. **American Family Physicians guidelines** for Acute Bacterial Prostatitis: Diagnosis and Management **2016**	N/A*

: *No updated versions available

1.1.1. Antimicrobial prescribing for urinary tract infections NICE guidelines published in October 2018

The below are missing recommendations from the NICE 2018 Pyelonephritis guidelines[3]. *Please refer to **Section 1.1** of CHI ABP original clinical guidance.*

- Self-care may, in addition to minor analgesics, include low-dose codeine for those over 12 years old.
- The first-line options for IV treatment are ciprofloxacin, levofloxacin, cefuroxime, ceftriaxone, gentamicin, and amikacin, which should only be used if the patient is unable to take oral antibiotics or is severely unwell.

- NICE notes that the European Medicines Agency has restricted the use of fluoroquinolones due to the risk of adverse effects on muscle, tendons, bones, and the CNS, but argues that their use is warranted for acute prostatitis because it is a severe infection that is associated with a risk of developing sepsis.

1.1.2. American Academy of Family Physicians (AAFP) 2016 Guidelines for Acute Bacterial Prostatitis: Diagnosis and Management

The recommendations provided below supplement the ones mentioned in the previous CHI ABP report. *Please refer to **Section 1.2** of CHI ABP original clinical guidance.*

These recommendations are accompanied by a grading scheme, outlined as follows[4]:

Table 3. AAFP 2016 Grading Scheme for Recommendations

Grading Scheme for Recommendations	
A	Consistent, good-quality patient-oriented evidence
B	Inconsistent or limited-quality patient-oriented evidence
C	Consensus, disease-oriented evidence, usual practice, expert opinion, or case series

The AAFP 2016 guidelines' recommendations are assigned the class of recommendations defined in the preceding table[4]:

- Blood cultures are indicated in patients with a body temperature greater than 101.1°F (38.4°C), a possible hematogenous source of infection (e.g., endocarditis with Staphylococcus aureus), or complicated infections (e.g., sepsis), and in patients who are immunocompromised (Evidence rating: C).

- Fevers that persist for longer than 36 hours should be evaluated with imaging to rule out prostatic abscess (Evidence rating: C).

- ABP occurring after a transrectal prostate biopsy should be treated with broad-spectrum antibiotics to cover fluoroquinolone-resistant bacteria and extended spectrum beta-lactamase–producing *E. coli* (Evidence rating: C).

1.2. Additional Guidelines

This section includes the added guidelines to the previous CHI ABP report, along with their recommendations. There are currently no Saudi guidelines for the management of ABP.

Table 4. List of the Additional Guidelines

Additional Guidelines
Asian Association of UTI & STI (AAUS) 2021 Guideline for Acute Bacterial Prostatitis
European Association of Urology (EAU) 2023 Guidelines on Urological Infections

1.2.1. Asian Association of UTI & STI (AAUS) 2021 Guideline for Acute Bacterial Prostatitis

The AAUS 2021 Guidelines' Grade of Recommendation and Levels of Evidence can be found in tables 5 and 6[8]:

Table 5. AAUS 2021 Guidelines' Grades of Recommendations

Grading Scheme for Recommendations	
Grade	**Nature of recommendations**
A	Based on clinical studies of good quality and consistency addressing the specific recommendations and including at least one randomized trial
B	Based on well-conducted clinical studies but without randomized clinical trials
C	Made despite the absence of directly applicable clinical studies of good quality

Table 6. AAUS 2021 Guidelines' Levels of Evidence

Grading Scheme for Recommendations	
Level	**Type of evidence**
1a	Evidence obtained from meta-analysis of randomized trials
1b	Evidence obtained from at least one randomized trial

2a	Evidence obtained from one well-designed controlled study without randomization
2b	Evidence obtained from at least one other type of well-designed quasi-experimental study
3	Evidence obtained from well-designed nonexperimental studies (e.g., comparative studies, correlation studies, and case reports)
4	Evidence obtained from expert committee reports or opinions or clinical experience of respected authorities

The guidelines recommend the following[8]:

- The AAUS 2021 guidelines for the management of ABP are based on guidelines published by the European Association of Urology, the Korean Society of Infectious Diseases/Korean Society for Chemotherapy, the National Institute for Health and Care Excellence, and the Japanese Association for Infectious Disease/Japanese Society of Chemotherapy.

- Rapid initiation of broad-spectrum parenteral antibiotics and symptomatic support are mandatory for patients with ABP (GR: B).

- Supportive measures include intravenous hydration and catheter drainage if the patient cannot void (GR: B).

- Insertion of a suprapubic cystostomy tube is the optimal therapy for relief from urinary obstruction (GR: B).

- In-and-out catheterization to relieve the initial obstruction or short term (<12 h) indwelling catheterization with a small-caliber Foley catheter is appropriate (GR: B).

- The selection and course of antibiotics should be adjusted according to the isolated pathogens and the results of bacterial susceptibility testing (GR: B).

- Prostatic abscess:
    - Suspicion of a developing abscess is raised if no response is noted in appropriate antibiotic therapy confirmed by TRUS (GR: B).
    - Initiation of broad-spectrum antibiotics and prompt surgical drainage is crucial if a prostatic abscess is discovered (GR: B).

- Hospitalization:

- Hospitalization should be considered in failed outpatient management, inability to tolerate oral intake, resistance risk factors, recent fluoroquinolone use, recent transurethral or transrectal prostatic manipulation, systemically ill or septicemia, and urinary (LE: 4).

- Pharmacological treatment:
  - In severe cases, parenteral administration of high doses of bactericidal antibiotics (e.g., a broad-spectrum penicillin derivative and a third-generation cephalosporin with or without aminoglycosides) or a fluoroquinolone is required until fever and other parameters of acute infection are normalized. (LE: 4).
  - An oral fluoroquinolone for 10 days may be sufficient in less severe cases (LE: 4).
  - The fever resolves in 36 to 48 hours in most cases (LE: 2a-4).
  - Oral antibiotic therapy should be continued at least for 2–4 weeks (LE: 4) although no consensus currently exists on optimal treatment duration.
  - The administration of cephalosporins or a quinolone alone or in combination with an aminoglycoside has been recommended (LE: 4).
  - Third-generation cephalosporins, a broad-spectrum beta-lactam/beta-lactamase inhibitor (BLI), or carbapenems are recommended for patients with ABP requiring hospitalization or if the resistance of the causative bacteria to fluoroquinolone is considered (LE: 4).
  - In the group of patients with prior manipulation in which pathogens other than *E. coli* constitute a substantial number of isolates, a combination of a cephalosporin and amikacin should be recommended for empirical therapy (GR: B).
  - With the high rate of fluoroquinolone resistance, cephalosporins with amikacin, carbapenems, or extended-spectrum penicillin with BLI should be considered as the preferred empirical ABP treatment in patients with history of prior urologic manipulation (LE: 4).
  - The use of levofloxacin could be an ABP risk factor after TRPB owing to an increase in fluoroquinolone-resistant E. coli in the rectum. Treatment with cephalosporin or carbapenem is recommended for patients with ABP after prostate biopsy (GR: C).
  - Carbapenem may be a treatment of choice for patients suspected of having sepsis (LE: 3).

- Other supportive treatment options such as alpha-blockers, antipyretics, or anti-inflammatory agents may be beneficial, although current data are insufficient. (LE: 3).
- Stool softeners are also recommended (GR: C).

1.2.2. European Association of Urology (EAU) 2023 Guidelines on Urological Infections

Please note that the recommendations for principles of treatment were developed using the GRADE approach[9]. Main recommendations are summarized below[5]:

- ABP should be treated according to the recommendations issued for complicated UTIs (strength rating: Strong).

- In case of hypersensitivity to penicillin, a cephalosporin can still be prescribed unless the patient has had systemic anaphylaxis in the past (LE: 2).

- In patients with a cUTI (including ABP) with systemic symptoms, empirical treatment should cover ESBL if there is an increased likelihood of ESBL infection based on prevalence in the community, earlier collected cultures and prior antimicrobial exposure of the patient (LE: 2).

- Intravenous levofloxacin 750 mg once daily for five days, is non-inferior to a seven-to-fourteen-day regimen of levofloxacin 500 mg once daily started intravenously and switched to an oral regimen (based on mitigation of clinical symptoms) (LE: 2).

- Use the combination of (Strength rating: Strong)
  - Amoxicillin plus an aminoglycoside.
  - A second-generation cephalosporin plus an aminoglycoside.
  - A third-generation cephalosporin intravenously as empirical treatment of complicated UTI with systemic symptoms.

- Only use ciprofloxacin provided that the local resistance percentages are < 10% when (Strength rating: Strong)
  - The entire treatment is given orally.
  - Patients do not require hospitalization.
  - Patient has an anaphylaxis for beta-lactam antimicrobials.

- Do not use ciprofloxacin and other fluoroquinolones for the empirical treatment of complicated UTI in patients from urology departments or

when patients have used fluoroquinolones in the last six months. (Strength rating: Strong)

- Manage any urological abnormality and/or underlying complicated factors. (Strength rating: Strong)

Section 2.0 Drug Therapy in Acute Bacterial Prostatitis

This section comprises three subsections: the first contains the newly recommended drugs, the second covers drug modifications, and the third outlines the drugs that have been withdrawn from the market.

2.1. Additions

No new drugs have been approved by the FDA or EMA for the treatment of acute bacterial prostatitis since February 2020.

2.2. Modifications

Below are the modifications made to the list of acute bacterial prostatitis drugs since the CHI report in February 2020, reflecting the changes and updates.

Table 7. Prescribing Edits Modifications of Drugs Used for the Management of Acute Bacterial Prostatitis

Drugs	PE modifications
Antibiotics with previous PA	**PA** was removed for all antibiotics listed.
Ciprofloxacin	**ST**: Ciprofloxacin is recommended as first-line treatment in the outpatient setting.
Ofloxacin	**ST**: Ofloxacin is recommended as first-line treatment in the outpatient setting.
Co-trimoxazole	**ST**: Co-trimoxazole should be reserved as a second-line treatment option in the outpatient setting for patients who are intolerant to fluoroquinolones.

Levofloxacin	**ST**: Levofloxacin should be reserved as a second-line treatment option in the outpatient setting.
Aminoglycosides	**Aminoglycosides: Amikacin, Gentamicin** **ST**: Part of the first-line treatment options – as IV antibiotics – in the inpatient setting.
Beta-lactams	**Cefepime, Ceftriaxone, Cefuroxime, Cefotaxime** **ST:** Part of the first-line treatment options – as IV antibiotics – in the inpatient setting.
Carbapenems	**ST**: First-line treatment option in case of ESBL infection.
Modification from previous CHI report	Men younger than 35 years who are sexually active and men older than 35 years who engage in high-risk sexual behavior should be treated with regimens that cover N. gonorrhoeae and C. trachomatis: - Ceftriaxone: IM: 500 mg as a single dose; 1 g is recommended for patients weighing ≥150 kg. Give in combination with treatment for chlamydia if it has not been excluded. When treatment failure is suspected (eg, detection of N. gonorrhoeae after treatment without additional sexual exposure), consult an infectious diseases specialist.[7] - Use cefixime only if ceftriaxone cannot be used because cefixime is not as effective → Oral: 800 mg as a single dose; give in combination with treatment for chlamydia if it has not been excluded. When treatment failure is suspected (eg, detection of N. gonorrhoeae after treatment without additional sexual exposure), consult an infectious diseases specialist.[7] For Urethral infection, empiric therapy for urethritis or pathogen-directed therapy for Chlamydia trachomatis: - Azithromycin can be used as an alternative agent → Oral: 1 g as a single dose, preferably under direct observation or 500 mg on day 1 then 250 mg once daily for 4 days (some experts prefer this dose for urethritis if adherence is not a concern); give in combination with ceftriaxone if there is microscopic evidence of gonococcal urethritis or if there is high clinical suspicion of gonococcal infection

2.3. Delisting

No medications have been withdrawn or are no longer recommended for the treatment of acute bacterial prostatitis since February 2020.

Section 3.0 Key Recommendations Synthesis

- The first-line options for IV treatment are ciprofloxacin, levofloxacin, cefuroxime, ceftriaxone, gentamicin, and amikacin, which should only be used if the patient is unable to take oral antibiotics or is severely unwell[3].

- Third-generation cephalosporins, a broad-spectrum beta-lactam/beta-lactamase inhibitor (BLI), or carbapenem are recommended for patients with ABP requiring hospitalization or if the resistance of the causative bacteria to fluoroquinolone is considered (LE: 4)[6].

- Acute bacterial prostatitis occurring after a transrectal prostate biopsy should be treated with broad-spectrum antibiotics to cover fluoroquinolone resistant bacteria and extended spectrum beta-lactamase–producing Escherichia coli (Evidence rating: C)[4].

- In patients with a cUTI (including ABP) with systemic symptoms, empirical treatment should cover ESBL if there is an increased likelihood of ESBL infection based on prevalence in the community, earlier collected cultures and prior antimicrobial exposure of the patient (LE: 2)[5].

- In patients with prior manipulation in which pathogens other than *E. coli* constitute a substantial number of isolates, combination of a cephalosporin and amikacin should be recommended for empirical therapy (GR: B)[6].

- Supportive measures include intravenous hydration and catheter drainage if the patient cannot void (GR: B)[6].

- Oral antibiotic therapy should be continued at least for 2–4 weeks (LE: 4) although no consensus currently exists on optimal treatment duration[6].

Section 4.0 Conclusion

This report serves as **an annex to the previous CHI Acute Bacterial Prostatitis report** and aims to provide recommendations to aid in the management of ABP. It is important to note that these recommendations should be utilized to support clinical

decision-making and not replace it in the management of individual patients with ABP. Health professionals are expected to consider this guidance alongside the specific needs, preferences, and values of their patients when exercising their judgment.

Section 5.0 References

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Section 6.0 Appendices

Appendix A. Prescribing Edits Definition

I. Prescribing Edits (ensure consistent use of abbreviations, e.g., CU, ST)

Some covered drugs may have additional requirements, rules, or limits on coverage. These requirements and limits may include:

Prescribing edits Tools	Description
AGE (Age):	Coverage may depend on patient age
CU (Concurrent Use):	Coverage may depend upon concurrent use of another drug
G (Gender):	Coverage may depend on patient gender
MD (Physician Specialty):	Coverage may depend on prescribing physician's specialty or board certification
PA (Prior Authorization):	Requires specific physician request process
QL (Quantity Limits):	Coverage may be limited to specific quantities per prescription and/or time period
ST (Step Therapy):	Coverage may depend on previous use of another drug
EU (Emergency Use only):	This drug status on Formulary is only for emergency use
PE (Protocol Edit):	Use of drug is dependent on protocol combination, doses, and sequence of therapy

Appendix B. Acute Bacterial Prostatitis Scope

Section	Rationale/Updates
Section 1.1.1 Prostatitis (acute): antimicrobial prescribing NICE guideline Published date: October 2018	**Antimicrobial prescribing for urinary tract infections NICE guidelines published in June 2019**[3] Additional Recommendations: • Self-care may, in addition to minor analgesics, include low-dose codeine for those over 12 years old • The first-line options for IV treatment are ciprofloxacin, levofloxacin, cefuroxime, ceftriaxone, gentamicin, and amikacin, which should only be used if the patient is unable to take oral antibiotics or is severely unwell. • NICE notes that the European Medicines Agency has restricted the use of fluoroquinolones due to the risk of adverse effects on muscle, tendons, bones, and the CNS, but argues that their use is warranted for acute prostatitis because it is a severe infection that is associated with a risk of developing sepsis.
Section 1.1.2 American Family Physicians guidelines for Acute Bacterial Prostatitis: Diagnosis and Management 2016 [4]	Missing Recommendations: • Blood cultures are indicated in patients with a body temperature greater than 101.1°F (38.4°C), a possible hematogenous source of infection (e.g., endocarditis with Staphylococcus aureus), or complicated infections (e.g., sepsis), and in patients who are immunocompromised (Evidence rating: C) • Fevers that persist for longer than 36 hours should be evaluated with imaging to rule out prostatic abscess. (Evidence rating: C) • Acute bacterial prostatitis occurring after a transrectal prostate biopsy should be treated with broad-spectrum antibiotics to cover fluoroquinolone resistant bacteria and extended spectrum beta-lactamase–producing Escherichia coli. (Evidence rating: C)
Section 1.1.3 AAUS guideline for acute bacterial prostatitis 2021 [8]	Please note that the current guidelines for ABP treatment have been worked out by the European Association of Urology, the Korean Society of Infectious Diseases/ Korean Society for Chemotherapy, the National Institute for Health and Care Excellence, and the Japanese Association for Infectious Disease/ Japanese Society of Chemotherapy.

	• Rapid initiation of broad-spectrum parenteral antibiotics and symptomatic support are mandatory for patients with ABP (GR: B). • Supportive measures include intravenous hydration and catheter drainage if the patient cannot void (GR: B). • Insertion of a suprapubic cystostomy tube is the optimal therapy for relief from urinary obstruction (GR: B). • In-and-out catheterization to relieve the initial obstruction or short term (<12 h) indwelling catheterization with a small-caliber Foley catheter is appropriate (GR: B). • The selection and course of antibiotics should be adjusted according to the isolated pathogens and the results of bacterial susceptibility testing (GR: B). Prostatic abscess: • Suspicion of a developing abscess is raised if no response is noted in appropriate antibiotic therapy confirmed by TRUS (GR: B). • Initiation of broad-spectrum antibiotics and prompt surgical drainage is crucial if a prostatic abscess is discovered (GR: B). Hospitalization: • Hospitalization should be considered in failed outpatient management, inability to tolerate oral intake, resistance risk factors, recent fluoroquinolone use, recent transurethral or transrectal prostatic manipulation, systemically ill or septicemia, and urinary (LE: 4). Pharmacological treatment: • In severe cases, parenteral administration of high doses of bactericidal antibiotics (e.g., a broad-spectrum penicillin derivative and a third-generation cephalosporin with or without aminoglycosides) or a fluoroquinolone is required until fever and other parameters of acute infection are normalized. (LE: 4). • An oral fluoroquinolone for 10 days may be sufficient in less severe cases (LE: 4).

	• The fever resolves in 36–48 h in most cases (LE: 2a-4). • Oral antibiotic therapy should be continued at least for 2–4 weeks (LE: 4) although no consensus currently exists on optimal treatment duration. • The administration of cephalosporins or a quinolone alone or in combination with an aminoglycoside has been recommended (LE: 4). • Third-generation cephalosporins, a broad-spectrum beta-lactam/beta-lactamase inhibitor (BLI), or carbapenem are recommended for patients with ABP requiring hospitalization or if the resistance of the causative bacteria to fluoroquinolone is considered (LE: 4). • In the group of patients with prior manipulation in which pathogens other than E. coli constitute a substantial number of isolates, a combination of cephalosporin and amikacin should be recommended for empirical therapy (GR: B). • With the high rate of fluoroquinolone resistance, cephalosporins with amikacin, carbapenems, or extended-spectrum penicillin with BLI should be considered as the preferred empirical ABP treatment in patients with history of prior urologic manipulation (LE: 4). • The use of levofloxacin could be an ABP risk factor after TRPB owing to an increase in fluoroquinolone-resistant E. coli in the rectum. Treatment with cephalosporin or carbapenem is recommended for patients with ABP after prostate biopsy (GR: C). • With the high rate of fluoroquinolone resistance, cephalosporins with amikacin, carbapenems, or extended-spectrum penicillin with BLI should be considered as the preferred empirical ABP treatment in patients with history of prior urologic manipulation (LE: 4). • Carbapenem may be a treatment of choice for patients suspected of having sepsis (LE: 3). • Other supportive treatment options such as alpha-blockers, antipyretics, or anti-inflammatory agents

	may be beneficial, although current data are insufficient. (LE: 3). • Stool softeners are also recommended (GR: C).
Section 1.1.4 **EAU Guidelines on Urological Infections 2023** [5]	• Treat acute bacterial prostatitis according to the recommendations for complicated UTIs (strength rating: Strong) • In the event of hypersensitivity to penicillin a cephalosporins can still be prescribed, unless the patient has had systemic anaphylaxis in the past. (LE: 2) • In patients with a cUTI (including ABP) with systemic symptoms, empirical treatment should cover ESBL if there is an increased likelihood of ESBL infection based on prevalence in the community, earlier collected cultures and prior antimicrobial exposure of the patient. (LE: 2) • Intravenous levofloxacin 750 mg once daily for five days, is non-inferior to a seven-to-fourteen-day regimen of levofloxacin 500 mg once daily starting intravenously and switched to an oral regimen (based on mitigation of clinical symptoms). (LE: 2) • Use the combination of: (Strength rating: Strong) - Amoxicillin plus an aminoglycoside. - A second-generation cephalosporin plus an aminoglycoside. - A third-generation cephalosporin intravenously as empirical treatment of complicated UTI with systemic symptoms. • Only use ciprofloxacin provided that the local resistance percentages are < 10% when; (strength rating: Strong) - The entire treatment is given orally. - Patients do not require hospitalization. - Patient has an anaphylaxis for beta-lactam antimicrobials. • Do not use ciprofloxacin and other fluoroquinolones for the empirical treatment of complicated UTI in patients from urology departments or when patients have used fluoroquinolones in the last six months. (Strength rating: Strong)

	• Manage any urological abnormality and/or underlying complicated factors. (Strength rating: Strong)
HTA Pharmacoeconomics Analysis	Recommendations from HTA bodies should be added under each drug therapy section as they are missing from the previous/initial document.

Appendix C. MeSH Terms PubMed

Query	filters	Search Details	Results
(((((Prostatitis[MeSH Terms]) OR (Acute Bacterial Prostatitis[Title/Abstract])) OR (Prostatitides[Title/Abstract])) OR (Acute Bacterial Prostatitides[Title/Abstract])) OR (Bacterial Prostatitides, Acute[Title/Abstract])) OR (Bacterial Prostatitis, Acute[Title/Abstract])	Guideline, from 2019 - 2023	("Prostatitis"[MeSH Terms] OR "acute bacterial prostatitis"[Title/Abstract] OR ((("Bacterial"[All Fields] OR "bacterially"[All Fields] OR "bacterials"[All Fields]) AND ("Prostatitis"[MeSH Terms] OR "Prostatitis"[All Fields])) AND "Acute"[Title/Abstract]) OR "bacterial prostatitis acute"[Title/Abstract]) AND ((guideline[Filter]) AND (2019:2023[pdat]))	2

Appendix D. Treatment Algorithm