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Drug Class Literature Scan: Cephalosporins

Date of Review: April 2026

Date of Last Review: January 2015
Literature Search: 10/01/14 – 01/21/26

Current Status of PDL Class:
See **Appendix 1**.

Plain Language Summary:

- Cephalosporins are medicines used to treat different types of infections caused by germs, also known as bacteria. They are commonly used for the treatment of skin infections and lung infections, like pneumonia.
- Guidelines published since the last review recommend cephalosporins as an initial treatment for Lyme disease rash (erythema migrans), pneumonia, infections that are spread by sexual contact, and foot infections in people that have diabetes.
- Evidence also recommends cephalosporins to treat infections after other antibiotics have been tried or in special circumstances, for example when someone has an antibiotic allergy or is pregnant. Examples of these types of conditions are urinary tract infections, ear infections, and skin infections.
- Providers are asked to prescribe a cephalosporin that is on the preferred drug list if it is a good choice for the patient. If a provider prescribes a non-preferred cephalosporin, they must explain to the Oregon Health Authority why the patient needs that medicine before Oregon Health Plan will pay for it. This is called prior authorization. The Drug Use Research and Management (DURM) group recommends making cefuroxime, cefaclor, and cefpodoxime preferred to increase access to therapies that are recommended by guidelines.

Conclusions:

- Cephalosporins are effective against gram negative, gram positive, and aerobic bacteria.[1] Oral cephalosporins are classified as first generation (i.e., cefadroxil, cephalexin, and cephradine), second generation (i.e., cefaclor, cefprozil, cefuroxime, and loracarbef) and third generation (i.e., cefdinir, cefixime, and cefpodoxime).[1] First generation cephalosporins are active against most gram-positive infections except for methicillin-resistant *Staphylococcus aureus* (MRSA) and penicillin-resistant *Streptococcus pneumoniae*. First generation agents are effective against *Escherichia coli, Proteus mirabilis, and Klebsiella pneumoniae*. Second generation cephalosporins have activity against *Haemophilus influenzae, Moraxella catarrhalis* and *Bacteroides*.[1] The third generation cephalosporins have less activity against gram-positive bacteria but are effective in treating Enterobacterales, *Neisseria sp.,* and *H. influenzae*. Ceftazidime, a third-generation cephalosporin, also has efficacy against *Pseudomonas aeruginosa*.
- Antimicrobial susceptibility data from 2024 and 2025 supplied by Oregon hospitals reported on 2 oral cephalosporins. Testing of samples shows cefazolin has high efficacy (85% or higher) against the following bacteria: *E. coli, K. pneumoniae*, *P. mirabilis*, *Staphylococcus aureus, Staphylococcus lugdunensis*, and *Streptococcus agalactiae* (Group B). Cefazolin has not shown to be effective against multi-drug resistant forms of the above bacteria. Cefpodoxime was effective for similar gram-negative bacteria as cefazolin and also had activity against *Enterobacter cloacae* complex and *Klebsiella oxytoca*. Susceptibility reporting on other oral cephalosporins was not provided.

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- This review identified 12 new guidelines for inclusion. Oral cephalosporins are recommended as first line treatment options for erythema migrans associated Lyme Disease (i.e., cefuroxime), severe cellulitis infections (i.e., cefuroxime), recurrent cystitis in pregnant women (i.e., cephalexin or cefaclor), community acquired pneumonia (CAP) in patients with risk factors (i.e., cefpodoxime or cefuroxime in combination with other antibiotics), mild diabetic foot infections (DFI) (i.e., cephalexin) and moderate to severe DFIs (i.e., cefuroxime).
- Guidance by the Infectious Disease Society of American (IDSA) for complicated urinary tract infections (cUTI) recommend the use of intravenous (IV) cephalosporins for patients with sepsis and oral therapy as a second line option in patients without sepsis.[2]
- A 2020 American Academy of Neurology (AAN)/American College of Rheumatology (ACR)/IDSA guideline recommends the use of oral cefuroxime for erythema migrans (circular skin rash) and IV cefuroxime for patients with neurological symptoms of Lyme disease or Lyme carditis.[3]
- Cephalexin is recommended by the National Institute for Health and Care Excellence (NICE) as a second-line treatment option for recurrent urinary tract infections (UTIs).[4]
- The NICE guidelines recommend the use of ceftriaxone for most cases of bacterial meningitis and meningococcal disease as empiric therapy and when susceptible causative organisms are identified.[5]
- When antibiotics are indicated, NICE recommends treatment of acute otitis media with amoxicillin first-line; however, there is no evidence of major treatment differences demonstrated between the penicillins, cephalosporins and macrolides.[6]
- For the treatment of cellulitis NICE recommends cefuroxime and ceftriaxone as options if infections are considered severe.[7]
- Guidance by NICE in a 2019 recommendation on the treatment of diverticulitis in adult patients recommends cephalexin with metronidazole as an alternative option to amoxicillin/clavulanate, if clinically indicated.[8] Most people with acute diverticulitis do not require antibiotic treatment.
- If IV therapy is indicated, cephalosporins are recommended by NICE for the prophylaxis and treatment of human and animal bites.[9]
- The European Association of Urology (EAU) 2025 guidelines recommend the use of cephalosporin in certain circumstances based on infecting organism, location, resistance patterns and adverse events.[10]
- The cephalosporins, cefuroxime and cefpodoxime, are recommended by the American Thoracic Society (ATS) and IDSA 2019 guidelines for the outpatient treatment of CAP for patients that have risk factors, such as diabetes or cancer.[11]
- First generation cephalosporins are recommended by the International Working Group on the Diabetic Foot (IWGDF)/IDSA 2023 for the treatment of mild DFI in patients that have no complicating features. For moderate to severe infections, second or third generation cephalosporins are recommended.[12]
- The Centers for Disease Control and Prevention (CDC) published guidelines for the treatment of sexually transmitted diseases (STD) in 2021.[13] The use of ceftriaxone intramuscular (IM) or IV is routinely recommended for the treatment of different types of Neisseria gonorrhoeae infections.[13]

Recommendations:

- Consider making cefuroxime, cefaclor and cefpodoxime preferred based on guideline recommendations.
- After evaluation of costs in executive session, make cefaclor capsules, cefadroxil capsules, and cefpodoxime tablets preferred.

Summary of Prior Reviews and Current Policy

- A previous review of the cephalosporins in 2015 found no difference in efficacy or safety between the cephalosporins within the same generation.
- A recommendation was implemented to offer at least one oral medication from each of the first, second and third generation cephalosporin classes to be preferred in addition to cefuroxime oral suspension due to cost effectiveness.
- Cephalexin capsules and suspension, cefprozil tablets and suspension, cefuroxime capsules and cefdinir capsules and suspension are preferred.
- Non-preferred products are subject to the general non-preferred drug prior authorization (PA) criteria.

Methods:
A Medline literature search for new systematic reviews and randomized controlled trials (RCTs) assessing clinically relevant outcomes to active controls, or placebo if needed, was conducted. Medline search strategy used for this literature scan is available in **Appendix 2**, which includes dates, search terms and limits used. The OHSU Drug Effectiveness Review Project, Agency for Healthcare Research and Quality (AHRQ), NICE, the Scottish Intercollegiate Guidelines Network (SIGN), and the Canada's Drug Agency (CDA-AMA) resources were manually searched for high quality and relevant systematic reviews. When necessary, systematic reviews are critically appraised for quality using the AMSTAR tool and clinical practice guidelines using the AGREE tool. The FDA website was searched for new drug approvals, indications, and pertinent safety alerts.

The primary focus of the evidence is on high quality systematic reviews and evidence-based guidelines. Randomized controlled trials will be emphasized if evidence is lacking or insufficient from those preferred sources.

New Systematic Reviews:
After review, 4 systematic reviews were excluded due to poor quality, wrong study design of included trials (e.g., observational), comparator (e.g., no control or placebo-controlled), or outcome studied (e.g., non-clinical).[14–17]

New Guidelines:
High Quality Guidelines:

IDSA – Management and Treatment of Complicated Urinary Tract Infections
A 2025 guidance from the IDSA updated previous recommendation for the treatment of cUTI.[2] The literature was searched from 2008 -2023. Older studies were excluded due to changing resistance patterns, in which results may not be applicable to current trends. Resistance rates were required to be reported to be included in the analysis. Recommendations for patients with sepsis, without sepsis and oral therapy will be presented.

For the empiric antibiotic treatment of cUTI, IDSA recommends specific treatment based on presence or absence of sepsis.[2] Outpatient management with oral therapy may be appropriate for some patients with pyelonephritis. Empiric therapy options are outlined in **Table 1**. Certain oral first or second generation-cephalosporins are recommended as alternative options in select settings for patient with cUTI without sepsis; however, they are less well studied and no specific therapy was recommended. Due to high resistance rates to fluoroquinolones and trimethoprim (TMP)/sulfamethoxazole (SMX), prior urine cultures are helpful if available.[2] In patients with cUTI and gram-negative infections, observational data has demonstrated that third-generation oral cephalosporins may have similar efficacy to fluoroquinolones or TMP-SMX. In patients with sepsis, antibiograms can be helpful to determine empiric therapy if it is local, recent and relevant to the patient (conditional recommendation; low quality of evidence).[2] Nitrofurantoin and oral fosfomycin are generally not recommended for cUTI because they may not achieve adequate levels in renal parenchyma and blood.

Table 1. IDSA Guidance for the Empiric Treatment of Complicated Urinary Tract Infection[2]

Indication	Preferred	Alternative	Strength of Recommendation
Sepsis with or without shock	Third- or fourth-generation cephalosporins (i.e., IV ceftriaxone, IV ceftazidime, IV	Novel beta lactam-beta lactamase inhibitors±; cefiderocol, plazomicin or older aminoglycosides+	Conditional recommendation; very low to moderate quality evidence. Moderate evidence for all classes except cephalosporins and older aminoglycosides which had very low quality of evidence.

	cefotaxime and IV cefepime), carbapenems*, piperacillin-tazobactam, fluoroquinolones^		
Without sepsis, IV route of therapy	Third- or fourth-generation cephalosporins (i.e., IV ceftriaxone, IV ceftazidime, IV cefotaxime and IV cefepime), piperacillin-tazobactam, fluoroquinolones^	Carbapenems*, newer agents (novel beta lactams-beta lactamase inhibitors, cefiderocol, plazomicin), or older aminoglycosides+.	Conditional recommendation; very low to moderate quality evidence. Moderate evidence for all classes except cephalosporins and older aminoglycosides which had very low quality of evidence.
Without sepsis, oral route of therapy	Fluoroquinolones^ or trimethoprim-sulfamethoxazole	Amoxicillin-clavulanate or oral cephalosporins (i.e., cefixime, cefpodoxime, cefuroxime, cephalexin)	Conditional recommendation; very low to moderate quality evidence. Moderate evidence for all classes except cephalosporins and older aminoglycosides which had very low quality of evidence.
Key: * Carbapenems recommended are imipenem-cilastatin, doripenem, meropenem and ertapenem; ^ Approved fluoroquinolones for UTI are ciprofloxacin and levofloxacin; + The older aminoglycosides recommended are gentamicin, amikacin, and tobramycin; ± Include ceftolozane-tazobactam, ceftazidime-avibactam, meropenem-vaborbactam, and imipenem-cilastatin-relebactam. Abbreviations: IV – intravenous; UTI – urinary tract infection.			

AAN/ACR/IDSA – 2020 Guidelines for the Prevention, Diagnosis, and Treatment of Lyme Disease

A multidisciplinary panel developed guidelines for managing Lyme disease. Methodology for the development of IDSA guidelines was followed to develop recommendations.[3] Antibiotic prophylaxis with a single doxycycline dose (200 mg for adults and 4.4 mg/kg for children up to 200 mg) is recommended for high-risk tick bites based on moderate-quality evidence (strong recommendation).[3] For those individuals with erythema migrans oral doxycycline (10 days), amoxicillin (14 days), or cefuroxime (14 days) is recommended (strong recommendation, moderate-quality of evidence).[3] Azithromycin 5-10 days can be used as a second-line agent.[3] In patients with neurological symptoms of Lyme disease without brain or spinal cord involvement, the recommendation is to treat the patient with IV ceftriaxone, cefotaxime, penicillin G, or oral doxycycline for a total of 14-21 days (strong recommendation, moderate-quality of evidence).[3] For patients with brain or spinal cord involvement related to Lyme disease, IV antibiotics are recommended over oral antibiotics (strong recommendation, moderate-quality of evidence). For the treatment of Lyme carditis 14-21 days of IV ceftriaxone is recommended, switching to an oral option (i.e., doxycycline, amoxicillin, cefuroxime, or azithromycin) when patient demonstrates clinical improvement (weak recommendation, very low-quality evidence).[3] If an initial course of oral antibiotics, in which a specific antibiotic was not recommended, is not effective at reducing Lyme arthritis, a 2–4-week course of IV ceftriaxone is recommended (weak recommendation, low-quality evidence).[3]

NICE – Recurrent Urinary Tract Infection: Antimicrobial Prescribing

The NICE updated guidance on the treatment of recurrent UTIs in 2024.[4] Behavioral and personal hygiene measures are recommended before routine antibiotic use. Underlying causes should also be ruled out.

If antibiotics are indicated, local antimicrobial resistance patterns should be considered. For patients who are 16 years and older, antiseptic prophylaxis with off-label methenamine hippurate, 1 g twice daily, may be used.[4] Recommended first-line antibiotic therapy includes: trimethoprim 200 mg single dose when exposed to trigger, or 100 mg at nightly, or nitrofurantoin 100 mg as a single dose when exposed to trigger, or 50 mg to 100 mg each night.[4] Second-line options include amoxicillin 500 mg single dose when exposed to trigger or 125 mg nightly or cephalexin 500 mg as a single dose when exposed to trigger or 125 mg each

night.[4] For those 16 years of age and younger, but older than 3 months, first choice antibiotics are trimethoprim and nitrofurantoin (see guidance for dosing).[4] Second-line treatments include amoxicillin (see guidance for dosing) and cephalexin 12.5 mg/kg at night with a maximum of 125 mg per dose.[4] Children under 3 months should be referred to a specialist. Treatment should be reassessed at least every 6 months.

NICE – Bacterial Meningitis and Meningococcal Disease

In March of 2024 NICE published recommendations for recognizing, diagnosing and managing bacterial meningitis and meningococcal disease.[5] The recommended treatment options will be covered in this review.

Intravenous ceftriaxone is recommended as empiric therapy for bacterial meningitis in the hospital. Cefotaxime, given IV, is recommended if ceftriaxone is contraindicated. Intravenous amoxicillin is recommended to be given with ceftriaxone or cefotaxime if the patient has risk factors for Listeria monocytogenes.[5] Antibiotics should be continued until testing suggests an alternative treatment is indicated. Ceftriaxone, or cefotaxime as an alternative, is recommended if it is known that *S. pneumoniae* is the causative organism.[5] Therapy for 10 days is recommended if the patient has recovered and if they have not recovered then an infection specialist should be consulted. If the causative organism is *H. influenzae* type b, ceftriaxone or alternatively cefotaxime if ceftriaxone is contraindicated, is recommended 7 days or up to 10 days if indicated.[5] Ceftriaxone, or cefotaxime if ceftriaxone is contraindicated, is recommended for 14 days for Group B *S Streptococcus* and an infection specialist consult is recommended.[5] If the meningitis is caused by *Enterobacterales*, ceftriaxone, or cefotaxime if ceftriaxone is contraindicated, is recommended for 21 days and an infection specialist should be consulted. *Neisseria meningitis* should be treated with 5 days of ceftriaxone, or cefotaxime if ceftriaxone is contraindicated.[5]

Intravenous ceftriaxone is recommended or confirmed meningococcal disease in the hospital. It should be given for 5 days if the patient has recovered, seek advice from an infection specialist if they have not recovered.[5]

NICE – Otitis Media Prescribing

National Institute for Health and Care Excellence updated guidance in March of 2022 for the use of antibiotics for otitis media.[6] Generally, most children and young people will not require antibiotics, as it has been shown that antibiotics have a small effect on symptom reduction. A back-up antibiotic prescription, only if needed, is recommended. Children under 2 years of age and those any age with otorrhea may be more likely to benefit from antibiotics.[6]

If antibiotics are prescribed, NICE found no differences between successful treatment rates of uncomplicated acute otitis media between the different classes of antibiotics (i.e., penicillins, cephalosporins, and macrolides), based on low- to moderate-quality evidence.[6] There is very low- to moderate-quality evidence that amoxicillin-clavulanate had significantly more adverse reactions compared to cephalosporins or azithromycin. Choice should be based on efforts to minimize resistance, such as choosing a narrow-spectrum antibiotic.[6] In general, amoxicillin (125 mg to 500 mg three times a day) should be offered first-line. Clarithromycin is an alternative first-line option. Amoxicillin-clavulanate is recommended as an appropriate second-line choice if symptoms worsen after first-choice antibiotic is administered for 2-3 days.[6] Five to seven days of antibiotic is recommended.[6]

NICE – Cellulitis and Erysipelas

Recommendations for the use of antibiotics in adults and children were updated in 2019 by NICE.[7] Antibiotic recommendations in adults 18 years and older are for flucloxacillin as first-line, which is not available in the US. Other first-line options are clarithromycin, erythromycin, and doxycycline. If the infection is near the eyes or nose then amoxicillin-clavulanate is recommended first-line or clarithromycin with metronidazole if amoxicillin-clavulanate is not an option.[7] For severe infections amoxicillin-clavulanate, cefuroxime, ceftriaxone or clindamycin is recommended. If MRSA is suspected or confirmed then a specialist may be

consulted for specific combination therapies from previously mentioned therapies. Vancomycin and linezolid may also be considered.[7] If the patient is pregnant, erythromycin is the preferred macrolide. Oral therapy should be used if infection severity does not require IV antibiotics. Up to 14 days of therapy may be required for full resolution of symptoms.

For children 1 month or older amoxicillin-clavulanate, clarithromycin, and erythromycin is recommended.[7] If the infection is near the eyes and nose amoxicillin-clavulanate is recommended first-line. Alternative options are clarithromycin with metronidazole, cefuroxime, and clindamycin. Vancomycin and linezolid are recommended for MRSA.[7]

NICE – Human and Animal Bite Treatment Recommendations

In 2020 NICE guidelines published treatment recommendations for adults and children with human or animal bites.[9] For patients 18 years and older give antibiotics for prophylaxis for 3 days and treatment for 5 days, with longer duration of therapy if clinically indicated. First-line treatment is amoxicillin/clavulanate 250/125 mg or 500/125 mg three times a day.[9] Alternative options are doxycycline 200 mg on the first day, then 100 mg or 200 mg daily with metronidazole 400 mg three times daily.[9] If IV antibiotics are indicated the first-choice is amoxicillin/clavulanate 1.2 grams three times day.[9] Alternative choices are cefuroxime 750 mg three times daily with metronidazole 500 mg three times daily or ceftriaxone 2 g daily with metronidazole 500 mg three times daily.[9] A specialist should be consulted for children less than one month. For children 1 month and older weight-based dosing of amoxicillin/clavulanate is recommended as the first-line treatment option. Alternative regimens are trimethoprim/sulfamethoxazole for children under 1 year and doxycycline with metronidazole for children 12-17 years.[9] Amoxicillin/clavulanate, cefuroxime with metronidazole, or ceftriaxone with metronidazole are recommended.[9]

NICE – Diverticular Disease

Guidance on the management and treatment of diverticulitis was published by NICE in 2019.[8] Antibiotics are not routinely recommended for treatment of this condition; however, antibiotics may be offered for patients with acute diverticulitis if they are systemically unwell, immunocompromised or they have significant comorbidities such as diabetes or uncontrolled hypertension. Intravenous antibiotics should be used for people with complicated acute diverticulitis that are admitted to the hospital.[8]

For adults, 18 years and older, amoxicillin/clavulanate is recommended first line for uncomplicated acute diverticulitis.[8] Five days of cephalexin with metronidazole and trimethoprim with metronidazole are recommended as alternative choices for acute diverticulitis. If the patient is diagnosed with complicated acute diverticulitis, recommendations include: IV amoxicillin/clavulanate, cefuroxime plus metronidazole, amoxicillin plus gentamicin and metronidazole, or ciprofloxacin plus metronidazole.[8] Up to 14 days of treatment may be needed for complicated infections and patients should be switched to oral therapy as soon as clinically appropriate.[8]

EAU – Urological Infections 2025

The EAU 2025 Guidelines provide updated recommendations for the use of antibiotics for urological infections.[10] Recommendations pertaining to antibiotic use will be presented. Evidence is graded from 1a (Highest Quality of Evidence) to 4 (Expert Opinion). Antibiotic selection should be guided by spectrum and susceptibility patterns, efficacy, tolerability, adverse reactions, costs and availability. Strength of recommendations range from Strong to Weak and are presented in **Table 2**. Cystitis is considered localized (i.e., no systemic infection in either sex) or systemic (i.e., pyelonephritis, prostatitis, etc.). Oral cephalosporins are not recommended for empiric therapy for cystitis due to risk of adverse effects on the environment (i.e., creating highly resistant organisms) and aminopenicillins are not recommended due to high resistance rates and increased selection for Extended-Spectrum Beta-Lactamase (ESBL)-producing

bacteria, but both can be used in select cases (Strong recommendation).[10] Fluoroquinolones should not be used unless it is considered inappropriate to use other antibiotics.

Table 2. EAU Antibiotic Recommendations for People with Urological Infections[10]

Diagnosis	Antibiotic Recommendation	Comments / Strength of Recommendation
Cystitis	Pivmecillinam 400 mg three times daily for 3-5 days	• First-line option in women / Strong
	Fosfomycin trometamol 3 g as a single dose	• First-line option in women / Strong
	Nitrofurantoin monohydrate/macrocrystal or nitrofurantoin macrocrystal prolonged release 100 mg twice daily for 5 days	• First-line option in women / Strong
	TMP/SMX 160/800 mg twice daily for 3 days or trimethoprim alone 200 mg twice daily for 5 days	• Alternative option • First choice only in areas with known resistance rates for *E.coli* of <20%
	Cephalosporins (e.g. cefadroxil 500 mg twice daily for 3 days)	• Other comparable cephalosporins can be used
	TMP/SMX or fluoroquinolone for at least 7 days	• First-line in men due to risk of prostate involvement
Cystitis in Pregnancy	Penicillins, cephalosporins, fosfomycin, nitrofurantoin, trimethoprim and sulphonamides can be considered	• Check for patient allergies • Trimethoprim should not be used in the first trimester of pregnancy and TMP/SMX is not recommended in the last trimester of pregnancy
Prevention of Recurrent Cystitis	Nitrofurantoin 50 mg or 100 mg once daily Fosfomycin trometamol 3 g once a week Trimethoprim 100 mg once daily	• No evidence of statistically significant difference in efficacy between antibiotics for recurrent cystitis
	Cephalexin 125 or 250 mg once daily Cefaclor 250 mg once daily	• Recommended for pregnant women with cystitis
Pyelonephritis (outpatient)	Fluoroquinolones (i.e., ciprofloxacin, levofloxacin) Cephalosporins (i.e., cefpodoxime, ceftibuten) TMP/SMX	• Fluoroquinolones are first-line / Strong • Only classes recommended for oral empirical therapy • If any class is used besides a fluoroquinolone, an initial intravenous dose of long-acting parenteral antimicrobial (e.g., ceftriaxone) should be used
Urethritis	Ceftriaxone and azithromycin for genitourinary urethritis	• Recommended first-line / Level 2a • Use nucleic acid amplification test (NAAT) to guide treatment
	Ceftriaxone 1-2 gm intramuscular or intravenously as a single dose Doxycycline 100 mg twice daily for 7 days	• For gonococcal infections
	Doxycycline 100 mg twice daily for 7 days	• For non-gonococcal infections (e.g., *Chlamydia trachomatis*)
	Azithromycin 1 gm day one and 500 mg days 2-4	• For *Mycoplasma genitalium*
	Doxycycline 100 mg twice daily for 7 days	• For *Ureaplasma urealyticum*
	Metronidazole 1.5-2 gm as a single dose	• For *Trichomonas vaginalis*

Acute Bacterial Prostatitis	Fluoroquinolone for 4-6 weeks	• First-line for empirical treatment
	Doxycycline 100 mg twice daily for 10 days	• Only for *C. trachomatis* or mycoplasma infections
	Azithromycin 500 mg once daily for up to 3 weeks	• Only for *C. trachomatis*
	Metronidazole 500 mg three times daily for 14 days	• Only for *T. vaginalis*
Chronic Bacterial Prostatitis	Fluoroquinolone	• First-line / Strong
	Doxycycline	• Only for *C. trachomatis*
	Macrolide	• If intra-cellular bacteria / Strong
	Metronidazole	• For *Trichomonas vaginalis* / Strong
Abbreviation: TMP/SMX – trimethoprim/sulfamethoxazole		

ATS – Treatment of Community-acquired Pneumonia

Guidelines for the diagnosis and treatment of adults with CAP were published in 2019 by the ATS and IDSA.[11] Treatment of CAP in the outpatient setting will be presented. Initial treatment strategies for patients with CAP are based on the presence or absence of additional risk factors **(Table 3)**.[11] There is no evidence demonstrating specific antibiotic regimens being superior or equivalent for the treatment of CAP. Duration of antibiotic therapy should be based on the clinical response of the patient but for no less than 5 days of treatment (strong recommendation, moderate quality of evidence).[11]

Table 3. Outpatient Initial Treatment of Community Acquired Pneumonia[11]

Patient Characteristics	Antibiotic Recommendation	Strength of Recommendation
If the patient has no comorbidities or risk factors for *methicillin-resistant Staphylococcus aureus* (MRSA) or *Pseudomonas aeruginosa*	• amoxicillin 1 gm 3 times a day	Strong recommendation, moderate quality of evidence
	• doxycycline 100 mg 2 times	Conditional recommendation, low quality of evidence
	• azithromycin 500 mg on day 1 and then 250 mg daily OR • clarithromycin 500 mg 2 times daily OR • clarithromycin ER 1,000 mg daily	Conditional recommendation, moderate quality of evidence - Only use macrolide if local pneumococcal resistance is <25%
If the patient has risk factors, such as chronic heart, lung, liver, renal disease, diabetes, alcoholism, asplenia or malignancy	*Combination Therapy* <u>Amoxicillin/clavulanate + Macrolide</u> • amoxicillin/clavulanate (dosed at 500 mg/125 mg 3 times daily, 875 mg/125 mg twice daily, or 2000 mg/125 mg twice daily) PLUS • azithromycin 500 mg on day 1 and 250 mg daily <u>Amoxicillin/clavulanate + Clarithromycin</u> • amoxicillin/clavulanate (dosed at 500 mg/125 mg 3 times daily, 875 mg/125 mg twice daily, or 2000 mg/125 mg twice daily) PLUS • clarithromycin 500 mg twice daily or extended release 1,000 mg daily	Strong recommendation, moderate quality of evidence (for all combinations except for those containing doxycycline) The recommendation for doxycycline is a conditional recommendation, low quality of evidence

	Amoxicillin/clavulanate + Doxycycline • amoxicillin/clavulanate (dosed at 500 mg/125 mg 3 times daily, 875 mg/125 mg twice daily, or 2000 mg/125 mg twice daily) PLUS • doxycycline 100 mg twice daily Cephalosporin + Macrolide • cefpodoxime 200 mg 2 times daily OR cefuroxime 500 mg 2 times daily PLUS • azithromycin 500 mg on day 1 and 250 mg daily Cephalosporin + Clarithromycin • cefpodoxime 200 mg 2 times daily OR cefuroxime 500 mg 2 times daily PLUS • clarithromycin 500 mg twice daily or extended release 1,000 mg daily OR Cephalosporin + Doxycycline • cefpodoxime 200 mg 2 times daily OR cefuroxime 500 mg 2 times daily PLUS • doxycycline 100 mg twice daily	
	Monotherapy • levofloxacin 750 mg daily • moxifloxacin 400 mg daily	Strong recommendation, moderate quality of evidence

IDSA – Diagnosis and Treatment of Diabetic Foot Infections

The IWGDF and IDSA published a guideline in 2023 on managing foot infections in patients with diabetes.[12] Recommendations related to treating DFI with antibiotics will be presented. Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) range from Strong (benefits clearly outweigh harm) or Weak/Conditional (benefits and risks are balanced) the certainty of evidence was designated from low to high.

Recommendations Pertaining to Treatment are as follows:

- Use systemic antibiotic regimens at standard dosing with evidence of efficacy to treat soft tissue infections in those with diabetes (Strong; High).[12]
- Antibiotics should be given for 1-2 weeks for DFI (Strong; High)[12]

- Antibiotic treatment duration of 3-4 weeks can be considered if the infection is improving, but extensive and slowly resolving or if the patient has peripheral arterial disease (PAD) (Conditional; Low).[12]
- The patient should receive additional diagnostic studies if the infection has not cleared after 4 weeks (Strong; Low).[12]
- Antibiotic selection should be based on the following (Best Practice Statement)[12]:
    - Likely or proven causative pathogen
    - Antibiotic susceptibility of the pathogen
    - Clinical severity of the infection
    - Evidence of efficacy of antibiotic for the treatment of DFI
    - Risk of adverse events, collateral damage of commensal flora, drug interactions, availability and cost.
- Only target gram-positive organisms (i.e., beta-hemolytic streptococci and *S. aureus*) in people with mild DFI who have not recently received antibiotic therapy and who reside in North America or Western Europe (Best Practice Statement).[12]
- Do not empirically target *P. aeruginosa* in temperate climates but use empirical treatment of *P. aeruginosa* if it has previously been isolated from the infection within the previous few weeks and the patient has a moderate to severe infection and live is Asia or North Africa (Best Practice Statement).[12]
- After minor amputation for diabetes related osteomyelitis of the foot and positive bone margin culture consider up to 3 weeks of antibiotics and up to 6 weeks for diabetes related foot osteomyelitis without bone resection or amputation (Conditional; Low).[12]

The most common causative pathogen of DFIs are gram-positive cocci (GPC) (i.e., staphylococci and streptococci).[12] Additional infecting organisms of concern are gram-negative rods (GNR) and strict anaerobes. For severe infections oral antibiotics are not recommended as initial therapy but may be considered for follow-on therapy after initial parenteral therapy. Antibiotic selection should be based on clinical trial evidence and suspected pathogen. Evidence has demonstrated that no antibiotic class has be found to be superior to another for DFI.[12] First generation cephalosporins (i.e., cephalexin) are recommended for mild DFI along with semisynthetic penicillinase-resistant penicillin (i.e., cloxacillin). For moderate or severe infections, second and third generation cephalosporins, such as cefuroxime, cefotaxime, ceftriaxone and ceftazidime are recommended, in addition to beta-lactam-beta lactamase inhibitors, semisynthetic penicillinase-resistant penicillins, glycopeptides, aminoglycosides, and carbapenems.[12]

CDC – Sexually Transmitted Infections Treatment Guidelines

In 2021 the CDC updated 2015 guidance on treating persons with STIs or who were at risk for them.[13] Updated recommendations pertaining to antibiotic use for the treatment of *Neisseria gonorrhoeae* was the only addition that pertained to this review. The use of cephalosporins will be discussed for treatment of STIs in which they are indicated.[13] Ceftriaxone IM or IV is most the most commonly recommended therapy for all types of gonococcal infections, as described below.

For the treatment of uncomplicated gonococcal infections of the cervix, urethra, or rectum ceftriaxone 500 mg IM for adults and adolescents weighing <150 kg.[13] A single dose of gentamicin 240 mg IM with azithromycin 2 grams orally or cefixime 800 mg orally can be given if ceftriaxone is not available. Ceftriaxone 500 mg IM as a single dose should be given for adults and adolescents weighing <150 kg (those weighing >150 kg should receive a 1 gram dose) with uncomplicated gonococcal infection of the pharynx.[13] Pregnant women with *N. gonorrhoeae* infections should be treated with ceftriaxone 500 mg as a single IM dose. If ceftriaxone cannot be used then an infectious disease specialist or STI clinical expert should be consulted. Ceftriaxone 1 gram IM should also be used for gonococcal conjunctivitis. Alternative options include cefotaxime 1 gram IV every 8 hours.[13] For gonococcal- related arthritis and arthritis-dermatitis syndrome ceftriaxone 1 gram IM or IV every 12 hours should be used.[13] Pelvic inflammatory disease (PID) is often caused by *N. gonorrhoeae* and *C. trachomatis*. For PID parenteral ceftriaxone 1 gram every 24 hours plus doxycycline 100 mg orally or IV every 12 hours plus metronidazole 500 mg. Cefotetan with doxycycline or cefoxitin with doxycycline are alternative regimens.[13] For women with mild to moderate PID therapy with ceftriaxone 500 mg IM as a single dose with

doxycycline and metronidazole can be considered. Alternative regimens include cefoxitin with probenecid, doxycycline or other parenteral third generation cephalosporins with doxycycline.

Neonates who are diagnosed with gonococcal ophthalmia neonatorum should receive ceftriaxone 25-50 mg/kg IV or IM as a single dose, but not more than 250 mg.[13] Those neonates infected with disseminated gonococcal infection should be treated with IV or IM ceftriaxone or cefotaxime for 7 days or 10-14 days if meningitis is documented. Neonates without signs of gonococcal infection that are born to mothers with untreated gonorrhea infections should receive ceftriaxone 20-50 mg/kg body weight IV or IM as a single dose, not to exceed 250 mg.[13] In children who weigh 45 kg or more should be treated with the adult regimen for uncomplicated gonococcal infections of the vulvovaginitis, cervicitis, urethritis, pharyngitis or proctitis. Children who weigh 45 kg or less should be given ceftriaxone 25-50 mg/kg IV or IM as a single dose and not to exceed 250 mg IM. For children 45 kg or less and are diagnosed with bacteremia or arthritis should be given ceftriaxone 50 mg/kg IM or IV as a single dose once daily for 7 days, with a maximum of 2 g daily dose.[13] For children weighing 45 kg or more the dose is ceftriaxone 1 gram IM or IV as a single dose daily for 7 days. For acute epididymitis, which is most likely caused by chlamydia or gonorrhea, ceftriaxone 500 mg IM as a single dose with doxycycline is recommended.

Ceftriaxone or levofloxacin are recommended for acute epididymitis caused by chlamydia, gonorrhea, or enteric organisms (men who practice insertive anal sex).[13] Acute proctitis should be managed with ceftriaxone 500 mg IM as single dose plus doxycycline. If a female adolescent or adult patient has been subject to sexual assault they should be given ceftriaxone 500 mg IM as a single dose plus doxycycline plus metronidazole. The same regimen, without the metronidazole, is recommended for adult male sexual assault victims.[13]

After review, two guidelines were excluded due to poor quality or lack of relevant guidance on topic.[18,19]

New Formulations:
None identified.

New FDA Safety Alerts:
None identified.

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Appendix 1: Current Preferred Drug List

First-generation

Generic	Brand	Form	PDL
cephalexin	CEPHALEXIN	CAPSULE	Y
cephalexin	CEPHALEXIN	SUSP RECON	Y
cefadroxil	CEFADROXIL	CAPSULE	N
cefadroxil	CEFADROXIL	SUSP RECON	N
cefadroxil	CEFADROXIL	TABLET	N
cephalexin	CEPHALEXIN	CAPSULE	N
cephalexin	CEPHALEXIN	TABLET	N

Second-generation

Generic	Brand	Form	PDL
cefprozil	CEFPROZIL	SUSP RECON	Y
cefprozil	CEFPROZIL	TABLET	Y
cefuroxime axetil	CEFUROXIME	TABLET	Y
cefaclor	CEFACLOR	CAPSULE	N
cefaclor	CEFACLOR	SUSP RECON	N
cefaclor	CEFACLOR ER	TAB ER 12H	N
loracarbef	LORABID	CAPSULE	N
loracarbef	LORABID	SUSP RECON	N

Third-generation

Generic	Brand	Form	PDL
cefdinir	CEFDINIR	CAPSULE	Y
cefdinir	CEFDINIR	SUSP RECON	Y
cefixime	CEFIXIME	CAPSULE	N
cefixime	CEFIXIME	SUSP RECON	N
cefpodoxime proxetil	CEFPODOXIME PROXETIL	SUSP RECON	N
cefpodoxime proxetil	CEFPODOXIME PROXETIL	TABLET	N

Appendix 2: New Comparative Clinical Trials

A total of 86 citations were manually reviewed from the initial literature search. After further review, all citations were excluded because of wrong study design (eg, observational), comparator (eg, no control or placebo-controlled), or outcome studied (eg, non-clinical).

Appendix 3: Medline Search Strategy

Database(s): **Ovid MEDLINE(R) ALL** 1946 to January 14, 2026

Search Strategy:

#	Searches	Results
1	cephalexin.mp. or Cephalexin/	4202
2	Cefadroxil/ or cefadroxil.mp.	831
3	cefprozil.mp. or Cefprozil/	349
4	Cefuroxime/ or cefuroxime.mp.	5990
5	Cefaclor/ or cefaclor.mp.	1934
6	loracarbef.mp.	209
7	Cefdinir/ or cefdinir.mp.	562
8	Cefixime/ or cefixime.mp.	2493
9	cefpodoxime.mp. or Cefpodoxime/	1009
10	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9	14666
11	limit 10 to (english language and humans)	7998
12	limit 11 to yr="2014 -Current"	2343
13	limit 12 to (clinical trial, phase iii or guideline or meta analysis or network meta-analysis or practice guideline or "systematic review")	86

Appendix 4: Key Inclusion Criteria

Population	Individuals with bacterial infections
Intervention	Cephalosporin antibiotics
Comparator	Antibiotic treatment other than cephalosporins
Outcomes	Infection cure rates
Setting	Outpatient