## *Therapeutic Class Overview*
## *Third Generation Cephalosporins*

**Therapeutic Class**

- **Overview/Summary:** This review will focus on the oral third generation cephalosporins.[1-7] The cephalosporin family of antibiotics is part of a larger group known as β-lactam antibiotics. Agents within this group share the structural feature of a β-lactam ring. The β-lactam antibiotics are generally considered bactericidal and work by inactivating enzymes involved with bacterial cell wall synthesis.[8] Cephalosporins cover a wide range of organisms and are frequently used antibacterial agents due to their spectrum of activity and ease of administration.[9] Cephalosporins are grouped into generations, based on their spectrum of activity. The first generation cephalosporins are active against gram-positive aerobes but are inactive against penicillin-resistant pneumococci. They typically have poor activity against gram-negative organisms, though some strains of *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis* and *Shigella* may be susceptible. Second generation cephalosporins have greater activity against *Haemophilus influenza* compared to the first generation cephalosporins and have enhanced activity against gram-negative bacteria in vitro. Third generation cephalosporins are active against streptococci, *Haemophilus influenza* and *Moraxella catarrhalis* and are more active against gram-negative bacilli compared to first or second generation cephalosporins; however, they are not as active against susceptible strains of staphylococci compared to first generation cephalosporins. Among the orally available third generation cephalosporins, cefpodoxime proxetil and cefdinir have more activity against staphylococci compared to cefixime and ceftibuten, while ceftibuten is weakly active against pneumococci. Its spectrum of activity is similar to cefdinir and cefpodoxime.[9,10] Fourth generation cephalosporins have enhanced activity against gram-negative bacteria compared to the first and second generation cephalosporins and have activity in vitro against gram-negative bacteria that are typically resistant to the third generation cephalosporins, including *Pseudomonas aeruginosa* and Enterobacteriaceae. In addition, they may be more active against gram-positive bacteria compared to some third generation cephalosporins. The only fourth generation cephalosporin is cefepime, which is only available parenterally. As a family, cephalosporins have poor activity against enterococci, Listeria and oxacillin-resistant staphylococci.[9,10] The cephalosporins reach therapeutic levels in urine and in pleural, pericardial, peritoneal and synovial fluid. With the exception of cefuroxime, the first and second generation cephalosporins are not able to effectively penetrate the cerebrospinal fluid and therefore should not be used to treat central nervous system infections. Conversely, the third generation cephalosporins do effectively penetrate the cerebrospinal fluid.[9] Clinical guidelines list third generation cephalosporins in different lines of therapy depending on type of infection, causative organicisms and other patient specific factors.[11-25]

**Table 1. Current Medications Available in the** Class[1-7]

| Generic (Trade Name) | Food and Drug Administration Approved Indications | Dosage Form/Strength | Generic Availability |
|---|---|---|---|
| Cefdinir* | Acute exacerbations of chronic bronchitis (bacterial), acute maxillary sinusitis, community-acquired pneumonia, otitis media, pharyngitis and/or tonsillitis, uncomplicated skin and skin structure infections | Capsule:<br>300 mg<br><br>Powder for oral suspension:<br>125 mg/5 mL<br>250 mg/5 mL | ✔ |
| Cefditoren (Spectracef®*) | Acute exacerbations of chronic bronchitis (bacterial), community-acquired pneumonia, pharyngitis and/or tonsillitis, uncomplicated skin and skin structure infections | Tablet:<br>200 mg<br>400 mg | ✔ |
| Cefixime (Suprax®) | Acute exacerbations of chronic bronchitis (bacterial), otitis media, pharyngitis and/or | Powder for oral suspension: | - |

| | | | |
|---|---|---|---|
| | tonsillitis, uncomplicated gonorrhea (cerfvical/urethral), uncomplicated urinary tract infections | 100 mg/5 mL<br>200 mg/5 mL<br><br>Tablet:<br>400 mg | |
| Cefpodoxime* | Acute ano-rectal infections in women, acute exacerbations of chronic bronchitis (bacterial), acute maxillary sinusitis, community-acquired pneumonia, otitis media, pharyngitis and/or tonsillitis, uncomplicated skin and skin structure infections, uncomplicated gonorrhea (cervical/urethral), uncomplicated urinary tract infections | Powder for oral suspension:<br>50 mg/5 mL<br>100 mg/5 mL<br><br>Tablet:<br>100 mg<br>200 mg | ✔ |
| Ceftibuten (Cedax®*) | Acute ano-rectal infections in women, otitis media, pharyngitis and/or tonsillitis | Capsule:<br>400 mg<br><br>Powder for oral suspension:<br>90 mg/5 mL<br>180 mg/5 mL | ✔ |

*Generic available in at least one dosage form or strength.

**Evidence-based Medicine**

- Studies evaluating the third generation cephalosporins for the treatment of acute exacerbations of chronic bronchitis have not consistently demonstrate significant differences in clinical response or eradication rate when compared to other cephalosporin agents.[26-31]
- Verghese and colleagues compared cefixime and cephalexin in the treatment of hospitalized patients with exacerbations of chronic bronchitis and demonstrated significantly better clinical cure rates in patients treated with cefixime compared to cephalexin (70.8 vs 50.0%; *P*<0.05). The incidence of diarrhea was higher in the cefixime group.[32]
- In the treatment of gonorrhea, cefixime and cefpodoxime have generally demonstrated comparable efficacy in the rate of bacteriologic cure (>90%) in open-label and dose-response studies, while cefixime has been shown to have comparable efficacy when compared to ceftriaxone.[33-37]
- Asmar et al compared cefixime and cefpodoxime in the treatment of acute otitis media. By day 15, the a bacteriologic cure was reported in 83 and 81% of patients treated with cefpodoxime and cefixime, respectively (*P*=0.541).[38]
- Casey et al conducted a study of high dose amoxicillin/clavulanic acid (10 day regimen) compared with a standard cefdinir regimen (5 days) and found that the clinical cure rate was statistically greater in the amoxicillin/clavulanic acid group (P=0.001).[66]
- Other head-to-head studies of the third generation cephalosporins in the treatment of acute otitis media demonstrated no statistically significant differences in efficacy between the agents.[60-65]
- Third generation cephalosporins have demonstrated their efficacy in the treatment of bacterial infections of acute bronchitis, chancroid and genital tract infections. [58-60]
- Studies evaluating the use of the third generation cephalosporins for the treatment of pharyngitis and/or tonsillitis have failed to consistently demonstrate “superiority” of any third generation cephalosporins over penicillin or amoxicillin.[39-46]
- In the treatment of lower respiratory tract infections including community-acquired pneumonia, no cephalosporin consistently demonstrated significant differences when the third generation cephalosporins were compared with each other or with cephalosporins in other generations.[47-49]
- Studies evaluating the treatment of skin and soft tissue infections, sinusitis and urinary tract infections did not consistently demonstrate the “superiority” of any third generation cephalosporins when compared with in-class or with other cephalosporins in other generations.[50-56]

**Key Points within the Medication Class**

- According to Current Clinical Guidelines:
    - Treatment guidelines identify third generation cephalosporins as alternative empiric agents for the treatment of community-acquired pneumonia, and as treatment options for infections due to *Enterobacteriaceae*.[11-14]
    - Third generation cephalosporins are considered alternative agents for the treatment of otitis media in patients with non-type 1 penicillin allergies and second-line agents for the treatment of sinusitis and pharyngitis due to penicillin and sulfamethoxazole/trimethoprim resistant bacteria or in patients with non-type 1 penicillin allergies.[15-17]
    - Cefixime is considered a second-line agent for the treatment of gonorrhea after ceftriaxone.[23]
    - The Global Initiative for Chronic Obstructive Lung Disease recommends the use a second or third generation cephalosporin as an alternative to penicillin, ampicillin, amoxicillin, tetracycline or sulfamethoxazole/trimethoprim in patients with chronic obstructive pulmonary disease and mild exacerbations with no risk of a poor outcome.[24]
    - For specific recommendations from current consensus guidelines, please refer to the full therapeutic class review.
- Other Key Facts:
    - Currently only cefixime (Suprax®) is only available as a branded agent. All other third generation cephalosporins are available generically in at least one dosage form or strength.
    - Only third generation cephalosporins that are available in an oral formulation are included within this review.

## References


1. Cefdinir capsules [package insert]. Dayton (NJ): Aurobindo Pharma USA, Inc.; 2014 Sep.
2. Cefdinir powder for suspension [package insert]. Dayton (NJ): Aurobindo Pharma USA, Inc.; 2014 Mar.
3. Spectracef® tablets [package insert]. Westmount (QC): Vansen Pharma Inc.; 2013 June.
4. Suprax® [package insert]. Baltimore (MD): Lupin Pharma; 2014 Sep.
5. Cefpodoxime tablets [package insert]. Princeton (NJ): Sandoz, Inc.; 2014 Jul.
6. Cefpodoxime granule for suspension [package insert]. Dayton (NJ): Aurobindo Pharma USA, Inc.; 2014 Mar.
7. Cedax® [package insert]. Gonzales (LA): Pernix Therapeutics, LLC; 2010 Apr.
8. Calderwood S. Beta-lactam antibiotics: Mechanisms of action and resistance and adverse effects. In: Hooper DC (Ed). UpToDate [database on the internet]. Waltham (MA): UpToDate; 2014 Apr. [cited 2014 Sep 15]. Available from: http://www.utdol.com/utd/index.do.
9. Calderwod S. Cephalosporins. In: Hooper DC (Ed). UpToDate [database on the internet]. Waltham (MA): UpToDate; 2014 Apr. [cited 2014 Sep 15]. Available from: http://www.utdol.com/utd/idex.do.
10. Antiinfectives 8:00, Antibacterials 8:12, Cephalosporins 8:12.06. In: McEvoy GK ed. American Hospital Formulary Services, AHFS Drug Information 2014 [monograph on the internet]. Bethesda (MD): American Society of Health-System Pharmacists; 2014 [cited 2014 Sep 15]. Available from: http://online.statref.com.
11. Mandell LA, Wunderink RG, Anzueto A, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis. 2007 Mar 1;44 Suppl 2:S27-72.
12. Ramsdell J, Narsavage GL, Fink JB; American College of Chest Physicians' Home Care Network Working Group. Management of community-acquired pneumonia in the home: an American College of Chest Physicians clinical position statement. Chest. 2005 May;127(5):1752-63.
13. Watkins RR, Lemonovich TL. Diagnosis and Management of Community-Acquired Pneumonia in Adults. Am Fam Physician. 2011 Jun 1;83(11):1299-1306.
14. Bradley JS, Byington CL, Shah SS, Alverson B, Carter ER, Harrisn C, et al. The Management of Community-Acquired Pneumonia in Infants and Children Older Than 3 Months of Age: Clinical Practice Guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. Clin Infect Dis. (2011) 53 (7): e25-e76. doi: 10.1093/cid/cir531
15. American Academy of Pediatrics Subcommittee on Management of Acute Otitis Media. Diagnosis and management of acute otitis media. Pediatrics. 2004 May;113(5):1451-65.
16. Shulman ST, Bisno AL, Clegg HW, Gerber MA, Kaplan EL, Lee Grace, et al. Clinical Practice Guideline for the Diagnosis and Management of Group A Streptococcal Pharyngitis: 2012 Update by the Infectious Diseases Society of America. Clin Infect Dis. (2012) doi: 10.1093/cid/cis629
17. Gerber M, Baltimore R, Eaton C, Gewitz M, Rowley A, Shulman S et al. Prevention of rheumatic fever and diagnosis and treatment of acute streptococcus pharyngitis: a scientific statement from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee of the Council on Cardiovascular Disease in the Young, the Interdisciplinary Council on Functional Genomics and Translational Biology, and the Interdisciplinary Council on Quality Care and Outcomes Research: Endorsed by the American Academy of Pediatrics. Circulation. 2009;119:1541-51.

18. Wald ER, Applegate KE, Bordley C, Darrow DH, Glode MP, Marcy M. Clinical Practice Guideline for the Diagnosis and Management of Acute Bacterial Sinusitis in Children Aged 1 to 18 Years. Pediatrics. 2013 Jul;132(1):e262-80.
19. Stevens DL, Bisno AL, Chambers HF, Dellinger EP, Goldstein EJC, Gorbach SL, et al. Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the Infectious Diseases Society of America. Clin Infect Dis. (2014) doi: 10.1093/cid/ciu296
20. Lipsky BA, Berendt AR, Cornia PB, Pile JC, Peters EJ, Armstrong DG, et al. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. Clin Infect Dis. 2012 Jun;54(12):e132-73.
21. American College of Obstetricians and Gynecologists Practice Bulletin: Treatment of urinary tract infections in nonpregnant women. Obstetrics and Gynecology. 2008;111(3):785-94.
22. Gupta K, Hooton TM, Naber KG, Wullt B, Colgan R, Miller LG, et al.; Infectious Diseases Society of America; European Society for Microbiology and Infectious Diseases. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: A 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. Clin Infect Dis. 2011 Mar;52(5):e103-20.
23. Centers for Disease Control and Prevention. Sexually Transmitted Diseases Treatment Guidelines, 2010. MMWR Morb Mortal Wkly Rep. 2010;59(No. RR-12):1-116. Available from: http://www.cdc.gov/std/treatment/2010/. Accessed Jul 31, 2012.
24. Vestbo J, Agusti AG, Anzueto A, Decramer M, Fabbri LM, Jones P, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease (updated 2014). [guideline on the internet]. Global Initiative for Chronic Obstructive Lung Disease, Inc.; 2013 [cited 2014 Sep 15]. Available from: http://www.goldcopd.org/uploads/users/files/GOLD_Report_2014_Jun11.pdf.
25. Bratzler DW, Houck PM; Surgical Infection Prevention Guidelines Writers Workgroup; Antimicrobial prophylaxis for surgery: an advisory statement from the National Surgical Infection Prevention Project. Clin Infect Dis. 2004 Jun 15;38(12):1706-15.
26. Phillips H, Van Hook CJ, Butler T, et al. A comparison of cefpodoxime proxetil and cefaclor in the treatment of acute exacerbation of COPD in adults. Chest. 1993;104(5):1387-91.
27. Chirurgi VA, Edelstein H, Oster SE, et al. Ceftibuten versus cefaclor for the treatment of bronchitis. J Antimicrob Chemother. 1991;28:577-80.
28. Fogarty CM, Bettis RB, Griffin TJ, Keyserling CH, Nemeth MA, Tack KJ. Comparison of a 5 day regimen of cefdinir with a 10 day regimen of cefprozil for treatment of acute exacerbation of chronic bronchitis. J Antimicrob Chemother. 2000;45:851-8.
29. Van Herwaarden C, Langan C, Siemon G, Rudolph C, Keyserling C, Nemeth M, et al. International study comparing cefdinir and cefuroxime axetil in the treatment of patients with acute exacerbation of chronic bronchitis. Int J Infect Dis. 1999;4:26-33.
30. Alvarez-Sala JL, Kardos P, Martínez-Beltrán J, Coronel P, Aguilar L. Clinical and bacteriological efficacy in treatment of acute exacerbations of chronic bronchitis with cefditoren-pivoxil versus cefuroxime-axetil. Antimicrob Agents Chemothera. 2006;50(5):1762-7.
31. Zuck P, Petitpretz P, Geslin P, Rio Y, Leblanc F. Bacteriological eradication of streptococcus pneumoniae from patients with acute exacerbations of chronic bronchitis: cefuroxime axetil versus cefixime. Int J Clin Prac. 1999;53(6):437-43.
32. Verghese A, Roberson D, Kalbfleisch JH, Sarubbi F. Randomized comparative study of cefixime versus cephalexin in acute bacterial exacerbations of chronic bronchitis. Antimicrob Agents Chemother. 1990;34(6):1041-4.
33. Handsfield H, McCormack W, Hook E, Douglas J, Covino J, Verdon M, et al. A comparison of single-dose cefixime with ceftriaxone as a treatment for uncomplicated gonorrhea. NEJM. 1991;325(19):1337-41.
34. Verdon M, Douglas J, Wiggins S, Handfield H. Treatment of uncomplicated gonorrhea with single doses of 200 mg cefixime. Sexually Transmitted Diseases. 1993;20(5):290-3.
35. Plourde P, Tyndall M, Agoki E, Ombette J, Slaney L, D'Costa L, et al. Single-dose cefixime versus single-dose ceftriaxone in the treatment of antimicrobial resistant Neisseria gonorrhoeae infection. Journal of Infectious Diseases. 1992;166(4):919-22.
36. Portilla I, Lutz B, Montalvo M, Mogabag W. Oral cefixime versus intramuscular ceftriaxone in patients with uncomplicated gonococcal infections. Sexually Transmitted Diseases. 1992;19(2):94-8.
37. Novak E, Paxton L, Tubbs H, Turner L, Keck C, Yatsu J. Orally administered cefpodoxime proxetil for treatment of uncomplicated gonococcal urethritis in males: a dose-response study. Antimicrobial agents and Chemotherapy. 1992;1764-5.
38. Asmar BI, Dajani AS, Del Beccaro MA, Mendelman PM. Comparison of cefpodoxime proxetil and cefixime in the treatment of acute otitis media in infants and children. Pediatrics. 1994;94(6):847-52.
39. Nemeth M, McCarty J, Gooch H, Henry D, Keyserling C, Tack K. Comparison of cefdinir and penicillin for the treatment of streptococcal pharyngitis. Clinical Therapeutics. 1999;21(11):1873-81.
40. Tack K, Henry D, Gooch W, Brink D, Keyserling C and the Cefdinir Pharyngitis Study Group. Five-day cefdinir treatment for streptococcal pharyngitis. Antimicrobial Agents and Chemotherapy. 1998;42(5):1073-5.
41. Brook I. A pooled comparison of cefdinir and penicillin in the treatment of group A beta-hemolytic streptococcal pharyngotonsillitis. Clin Therap. 2005;27(8):1266-73.
42. Ozaki T, Nishimura N, Suzuki M, Narita A, Watanabe N, Ahn J, et al. Five-day oral cefditoren pivoxil versus 10-day oral amoxicillin for pediatric group A streptococcal pharyngotonsillitis. J Infect Chemother. 2008;14:213-8.
43. Block S, Hedrick J, Tyler R. Comparative study of the effectiveness of cefixime and penicillin V for the treatment of streptococcal pharyngitis in children and adolescents. Pediatr Infect Dis J. 1992;11:919-25.
44. Adam D, Cefixime Study Group, Hostalek U, Troster K. 5-day cefixime therapy for bacterial pharyngitis and/or tonsillitis: comparison with 10-day penicillin V therapy. Infection. 1995;23(Suppl 2):S83-6.
45. Pichichero ME, Gooch WM, Rodriguez W, Blumer JL, Aronoff SC, Jacobs RF, et al. Effective short-course treatment of acute group A beta-hemolytic streptococcal tonsillopharyngitis. Arch Pediatr Adolesc Med. 1994;148:1053-60.
46. Pichichero M, McLinn S, Gooch M, Rodriguez M, Goldfarb J, Reidenberg B, et al. Ceftibuten vs. penicillin V in group A beta-hemolytic streptococcal pharyngitis. Pediatr Infect Dis J. 1995;14:S102-7.

47. van Zyle L, le Roux J, LaFata J, Volk R, Palo W, Flamm R, et al. Cefditoren pivoxil versus cefpodoxime proxetil for community-acquired pneumonia: results from a multi-center, prospective, randomized, double-blind study. Clin Therap. 2002;24(11):1840-53.
48. Drehobl M, Bianchi P, Keyserling CH, Tack KJ, Griffin TJ. Comparison of cefdinir and cefaclor in the treatment of community-acquired pneumonia. Antimicrob Agents Chemother. 1997;41(7):1579-83.
49. Sengupta J, Mondal AK, Jain P, Garg RD, Mathur NC, Moharana AK. Comparative evaluations of cefpodoxime versus cefixime in children with lower respiratory tract infections. Indian J Pediatr. 2004;71(6):517-21.
50. Tack KJ, Keyserling CH, McCarty J, Hedrick JA. Study of use of cefdinir versus cephalexin for treatment of skin infections in pediatric patients. Antimicrob Agents and Chemother. 1997;41(4):739-42.
51. Tack K, Littlejohn T, Mailloux G, Wolf M, Keyserling C. Cefdinir versus cephalexin for the treatment of skin and skin structure infections. Clin Therap. 1998;20(2):244-56.
52. Stevens DL, Pien F, Drehobol M. Comparison of oral cefpodoxime proxetil and cefaclor in the treatment of skin and soft tissue infections. Diagn Microbiol Infect Dis. 1993;16:123-9.
53. Bucko AD, Hunt BJ, Kidd SL, Hom R. Randomized, double-blind, multicenter comparison of oral cefditoren 200 or 400 mg BID with either cefuroxime 250 mg BID or cefadroxil 500 mg BID for the treatment of uncomplicated skin and skin-structure infections. Clin Ther. 2002;27(7):1134-47.
54. Gehanno P, Depondt J, Barry B, Simonet M, Dewever H. Comparison of cefpodoxime proxetil with cefaclor in the treatment of sinusitis. J Antimicrob Chemother. 1990;26(Suppl E): 87-91.
55. Leigh AP, Nemeth MA, Keyserling CH, Hotary LH, Tack KJ. Cefdinir versus cefaclor in the treatment of uncomplicated urinary tract infection. Clin Ther. 2000;22(7):818-25.
56. Ho MW, Wang FD, Fung CP, Liu CY. Comparative study of ceftibuten and cefixime in the treatment of complicated urinary tract infections. J Microbiol Immunol Infect. 2001;34:185-9.
57. Ziering W, McElvaine P. Randomized comparison of once-daily ceftibuten and twice daily clarithromycin in the treatment of acute exacerbations of chronic bronchitis. Infection 1998;26(1):68-75.
58. Martin DH, Sargent SJ, Wendel GD Jr, McCormack WM, Spier NA, Johnson RB. Comparison of azithromycin and ceftriaxone for the treatment of chancroid. Clin Infect Dis. 1995;21:409-14.
59. French LM, Smaill FM. Antibiotic regimens for endometritis after delivery. Cochrane Database Syst Rev. 2004;18(4):CD001067.
60. Piippo T, Stefansson S, Pitkäjärvi T, Lundberg C. Double-blind comparison of cefixime and cefaclor in the treatment of acute otitis media in children. Scand J Infect Dis. 1991;23:459-65.
61. MacLoughlin GJ, Barreto DG, de la Torre C, Pinetta EA, del Castillo F, Palma L. Cefpodoxime proxetil suspension compared with cefaclor suspension for treatment of acute otitis media in pediatric patients. J Antimicrob Chemother. 1996;37:565-73.
62. Blumer JL, McLinn SE, Deabate A, et al. Multinational multicenter controlled trial comparing ceftibuten with cefaclor for the treatment of acute otitis media. Pediatr Infect Dis J. 1995;14:S115-20.
63. Blumer JL, Mclinn SE, Deabate CA, Kafetzis DA, Perrotta RJ, Salgado O. Five-day cefdinir course vs ten-day cefprozil course for treatment of acute otitis media. Pediatr Infect Dis J. 2000;19(12):S147-S52.
64. Block S, Cifaldi M, Gu Y, Paris M. A comparison of 5 days of therapy with cefdinir or azithromycin in children with acute otitis media: a multicenter, prospective single-blind study. Clin Therap. 2005;27(6):786-94.
65. Mandel E, Rockette H, Paradise J, Bluestone C, Nozza R. Comparative efficacy of erythromycin-sulfisoxazole, cefaclor, amoxicillin or placebo for otitis media with effusion on children. Pediatr Infect Dis J. 1991;10:899-906.
66. Casey JR, Block SL, Hedrick J, Almudevar A, Pichichero M. Comparison of Amoxicillin/Clavulanic Acid High Dose with Cefdinir in the Treatment of Acute Otitis Media. Drugs. 2012 Oct 22;72(15):1991-7. doi: 10.2165/11590320-000000000-00000.
67. Song F, Glenny AM. Antimicrobial prophylaxis in colorectal surgery: a systematic review of randomized controlled trials. Br J Surg. 1998 Sep;85(9):1232-41.
68. Zalmanovici Trestioreanu A, Green H, Paul M, Yaphe J, Leibovici L. Antimicrobial agents for treating uncomplicated urinary tract infection in women. Cochrane Database Syst Rev. 2010 Oct 6;(10):CD007182
69. Bocquet N, Sergent Alaoui A, Jais JP, Gajdos V, Guigonis V, Lacour B, et al. Randomized trial of oral versus sequential IV/oral antibiotic for acute pyelonephritis in children. Pediatrics. 2012 Feb;129(2):e269-75.
70. Hooton TM, Roberts PL, Stapleton AE. Cefpodoxime vs ciprofloxacin for short-course treatment of acute uncomplicated cystitis: a randomized trial. JAMA. 2012 Feb 8;307(6):583-9.
71. Falagas ME, Siempos II, Vardakas KZ. Linezolid versus glycopeptide or beta-lactam for treatment of Gram-positive bacterial infections: meta-analysis of randomized controlled trials. Lancet Infect Dis. 2008 Jan;8(1):53-66.

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# *Third Generation Cephalosporins*

## Overview/Summary

The cephalosporin family of antibiotics is part of a larger group known as β-lactam antibiotics. This review will focus on the oral third generation cephalosporins.[1-7] Agents within this group share the structural feature of a β-lactam ring. The β-lactam antibiotics are generally considered bactericidal and work by inactivating enzymes involved with bacterial cell wall synthesis.[8] Cephalosporins cover a wide range of organisms and are frequently used antibacterial agents due to their spectrum of activity and ease of administration.[9]

Cephalosporins are grouped into generations, based on their spectrum of activity. The first generation cephalosporins are active against gram-positive aerobes but are inactive against penicillin-resistant pneumococci. They typically have poor activity against gram-negative organisms, though some strains of *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis* and *Shigella* may be susceptible. Second generation cephalosporins have greater activity against *Haemophilus influenza* compared to the first generation cephalosporins and have enhanced activity against gram-negative bacteria in vitro. Third generation cephalosporins are active against streptococci, *Haemophilus influenza* and *Moraxella catarrhalis* and are more active against gram-negative bacilli compared to first or second generation cephalosporins; however, they are not as active against susceptible strains of staphylococci compared to first generation cephalosporins. Among the orally available third generation cephalosporins, cefpodoxime proxetil and cefdinir have more activity against staphylococci compared to cefixime and ceftibuten, while ceftibuten is weakly active against pneumococci. Its spectrum of activity is similar to cefdinir and cefpodoxime.[9,10] Fourth generation cephalosporins have enhanced activity against gram-negative bacteria compared to the first and second generation cephalosporins and have activity in vitro against gram-negative bacteria that are typically resistant to the third generation cephalosporins, including *Pseudomonas aeruginosa* and Enterobacteriaceae. In addition, they may be more active against gram-positive bacteria compared to some third generation cephalosporins. The only fourth generation cephalosporin is cefepime, which is only available parenterally. As a family, cephalosporins have poor activity against enterococci, Listeria and oxacillin-resistant staphylococci.[9,10]

Collectively, the cephalosporins are able to reach therapeutic levels in urine and in pleural, pericardial, peritoneal and synovial fluid. With the exception of cefuroxime, the first and second generation cephalosporins are not able to effectively penetrate the cerebrospinal fluid and therefore should not be used to treat central nervous system infections. Conversely, the third generation cephalosporins do effectively penetrate the cerebrospinal fluid.[9] Current clinical guidelines for infections are listed in Table 11.[11-25]

Currently cefixime (Suprax®) is the only agent that does not have a generic option in at least one dosage form or strength.

## Medications

**Table 1. Medications Included Within Class Review**

| Generic Name (Trade name) | Medication Class | Generic Availability |
|---|---|---|
| Cefdinir* | Third generation cephalosporin | ✔ |
| Cefditoren (Spectracef®*) | Third generation cephalosporin | ✔ |
| Cefixime (Suprax®) | Third generation cephalosporin | - |
| Cefpodoxime* | Third generation cephalosporin | ✔ |
| Ceftibuten (Cedax®*) | Third generation cephalosporin | ✔ |

*Generic available in at least one dosage form or strength.

The third generation cephalosporins have been shown to be active against the strains of microorganisms indicated in Table 2. This activity has been demonstrated in clinical infections and is represented by the Food and Drug Administration-approved indications for the third generation cephalosporins that are noted in Table 3. The third generation cephalosporins may also have been found to show activity to other microorganisms in vitro; however, the clinical significance of this is unknown since their safety and efficacy in treating clinical infections due to these microorganisms have not been established in adequate and well-controlled trials. Although empiric antibacterial therapy may be initiated before culture and susceptibility test results are known, once results become available, appropriate therapy should be selected.

**Table 2. Microorganisms Susceptible to the Third Generation Cephalosporins**[1-7]

| Bacteria | Cefdinir | Cefditoren | Cefixime | Cefpodoxime | Ceftibuten |
|---|---|---|---|---|---|
| **Gram-Positive Aerobes** | | | | | |
| *Staphylococcus aureus* | ✔ *,¶ | ✔ *,¶ | | ✔ *,¶ | |
| *Staphylococcus saprophyticus* | | | | ✔ | |
| *Streptococcus pneumoniae* | ✔ † | ✔ † | ✔ † | ✔ † | ✔ † |
| *Streptococcus pyogenes* | ✔ | ✔ | ✔ | ✔ | ✔ |
| **Gram-Negative Aerobes** | | | | | |
| *Escherichia coli* | | | ✔ | ✔ | |
| *Haemophilus influenzae* | ✔ * | ✔ * | ✔ * | ✔ *,§ | ✔ * |
| *Haemophilus parainfluenzae* | ✔ * | ✔ * | | | |
| *Klebsiella* spp. | | | | ✔ | |
| *Moraxella (Branhamella) catarrhalis* | ✔ * | ✔ * | ✔ * | ✔ * | ✔ * |
| *Neisseria gonorrhoeae* | | | ✔ ‖ | ✔ ‖ | |
| *Proteus mirabilis* | | | ✔ | ✔ | |

*Including β-lactamase producing strains.
†Penicillin-susceptible strains only.
‡β-lactamase positive and negative strains.
§Only non-β-lactamase producing strains for the treatment of acute bacterial exacerbations of chronic bronchitis.
‖Including penicillinase-producing strains.
¶Inactive against MRSA

## Indications

**Table 3. Food and Drug Administration (FDA)-Approved Indications**[1-7]

| Indication | Cefdinir | Cefditoren | Cefixime | Cefpodoxime | Ceftibuten |
|---|---|---|---|---|---|
| **Dermatologic** | | | | | |
| Uncomplicated skin and skin structure infections | ✔ | ✔ | | ✔ | |
| **Genitourinary** | | | | | |
| Acute ano-rectal infections in women | | | | ✔ | |
| Gonorrhea, uncomplicated (cervical/urethral) | | | ✔ | ✔ | |
| Uncomplicated urinary tract infections | | | ✔ | ✔ | |
| **Respiratory** | | | | | |
| Acute exacerbations of chronic bronchitis (bacterial) | ✔ | ✔ | ✔ | ✔ | ✔ |
| Acute maxillary sinusitis | ✔ | | | ✔ | |
| Community-acquired pneumonia | ✔ | ✔ | | ✔ | |
| Otitis media | ✔ | | ✔ | ✔ | ✔ |
| Pharyngitis and/or tonsillitis | ✔ | ✔ | ✔ | ✔ | ✔ |

## Pharmacokinetics

**Table 4. Pharmacokinetics**[1-7]

| Generic Name | Time to Peak Blood Levels (hours) | Protein Binding (%) | Renal Excretion (%) | Serum Half-Life (hours) |
|---|---|---|---|---|
| Cefdinir | 2 to 4 | 60 to 70 | 11.6 to 18.4 | 1.7 |
| Cefditoren | 1.5 to 3.0 | 88 | 16 to 22 | 1.6 |
| Cefixime | 2 to 6 | 65 | 50 | 3 to 9 |
| Cefpodoxime | 2 to 3 | 21 to 29 | 29 to 33 | 2.0 to 2.8 |
| Ceftibuten | 2.0 to 2.6 | 65 | 56 | 2.0 to 2.4 |

## Clinical Trials

The clinical studies demonstrating the safety and efficacy of the third generation cephalosporins in their respective Food and Drug Administration-approved indications are listed in Table 5.[26-71]

Studies evaluating the third generation cephalosporins for the treatment of acute exacerbations of chronic bronchitis did not consistently demonstrate significant differences in clinical response or eradication rate when compared to other cephalosporin agents.[26-31] Verghese and colleagues compared cefixime and cephalexin in the treatment of hospitalized patients with exacerbations of chronic bronchitis and demonstrated significantly better clinical cure rates in patients treated with cefixime compared to cephalexin (70.8 vs 50.0%; P<0.05). The incidence of diarrhea was higher in the cefixime group.[32] In the treatment of gonorrhea, cefixime and cefpodoxime have generally demonstrated comparable efficacy in the rate of bacteriologic cure (>90%) in open-label and dose-response studies, while cefixime has been shown to have comparable efficacy when compared to ceftriaxone.[33-37]

Asmar et al compared cefixime and cefpodoxime in the treatment of acute otitis media. By day 15, the a bacteriologic cure was reported in 83 and 81% of patients treated with cefpodoxime and cefixime, respectively (P=0.541).[38] Casey et al conducted a study evaluating cure rates of otitis media in young patients six to 24 months of age. A high dose amoxicillin/clavulanic acid (10 day regimen) was compared to a cefdinir regimen (five days). The clinical cure rate with amoxicillin/clavulanic acid high dose (86.5%) was significantly higher than that with cefdinir (71.0%; P=0.001).[66] Other head-to-head studies of the third generation cephalosporins in the treatment of acute otitis media demonstrated no statistically significant differences in efficacy between the agents. [60-63] Studies evaluating the use of the third generation cephalosporins for the treatment of pharyngitis and/or tonsillitis have failed to consistently demonstrate "superiority" of any third generation cephalosporins over penicillin or amoxicillin.[39-46] In the treatment of lower respiratory tract infections including community-acquired pneumonia, no cephalosporin consistently demonstrated significant differences when the third generation cephalosporins were compared with each other or with cephalosporins in other generations.[46-49]

Studies evaluating the treatment of skin and soft tissue infections, sinusitis and urinary tract infections did not consistently demonstrate the "superiority" of any third generation cephalosporins when compared with in-class or with other cephalosporins in other generations.[50-56]

**Table 5. Clinical Trials**

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
|---|---|---|---|---|
| **Acute Bacterial Exacerbations of Chronic Bronchitis and Secondary Bacterial Infections of Acute Bronchitis** | | | | |
| Phillips et al[26]<br><br>Cefaclor 250 mg TID<br><br>vs<br><br>cefpodoxime 200 mg BID | DB, MC, RCT<br><br>Patients with signs and symptoms of acute bacterial exacerbation of COPD | N=301<br><br>10 days | Primary:<br>Clinical evaluations, microbiologic evaluations<br><br>Secondary:<br>Adverse events | Primary:<br>There were no statistically significant differences between cefpodoxime and cefaclor in the eradication of the original pathogen (91 vs 92%, respectively; no *P* value reported) or in clinical response at three to seven days post-treatment (99 vs 92%, respectively; *P* value not reported).<br><br>More bacterial isolates were susceptible to cefpodoxime compared to cefaclor (91 vs 84%, respectively; *P*<0.001).<br><br>Secondary:<br>There were no statistically significant differences between cefpodoxime and cefaclor in adverse events (11 vs 12%, respectively; *P* value not reported). |
| Chirurgi et al[27]<br><br>Cefaclor 250 mg every 8 hours<br><br>vs<br><br>ceftibuten 400 mg QD | PRO, RCT<br><br>Patients with acute bronchitis, not pneumonia | N=45<br><br>Unspecified (from 7 to 14 days) | Primary:<br>Clinical efficacy, bacteriologic efficacy<br><br>Secondary:<br>Adverse events | Primary:<br>Clinical efficacy was reported as 87.5 and 92.3% of patients treated with ceftibuten and cefaclor, respectively (*P* value not reported). Bacteriologic efficacy was reported as 87.5 and 80.0% of patients treated with ceftibuten and cefaclor, respectively (*P* value not reported).<br><br>Secondary:<br>The rates of adverse events were reported as 7.9 and 5.6% in patients treated with ceftibuten and cefaclor, respectively (*P* value not reported). |
| Fogarty et al[28]<br><br>Cefprozil 500 mg BID (for 10 days)<br><br>vs<br><br>cefdinir 300 m BID (for 5 days) | DB, MC, PRO, RCT<br><br>Patients with acute exacerbations of chronic bronchitis | N=281<br><br>5 to 10 days | Primary:<br>Clinical evaluations, microbiologic evaluations<br><br>Secondary:<br>Adverse events | Primary:<br>Seven to eleven days after the patient had stopped therapy, clinical cure rates were reported as 80 and 72% for patients treated with cefdinir and cefprozil, respectively (*P* value not reported).<br><br>Seven to eleven days after the patient had stopped therapy, microbiological eradication rates were reported as 81 and 84% for patients treated with cefdinir and cefprozil, respectively (*P* value not reported).<br><br>Secondary:<br>Patients treated with cefdinir experienced more cases of mild diarrhea than patients treated with cefprozil (17 vs 6%, respectively; *P*<0.01). |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
|---|---|---|---|---|
| Van Herwaarden et al[29]<br><br>Cefdinir 600 mg QD<br><br>vs<br><br>cefdinir 300 mg BID<br><br>vs<br><br>cefuroxime 250 mg BID | DB, MC, PG, RCT<br><br>Patients 13 years of age and older with a history of chronic bronchitis and a current diagnosis of an acute exacerbation of chronic bronchitis | N=1,045<br><br>Up to 35 days post-treatment | Primary:<br>Clinical response rate, microbiological eradication<br><br>Secondary:<br>Appearance of new pathogens during or after treatment | Primary:<br>The clinical response rates for the cefdinir QD, cefdinir BID and cefuroxime groups were 81, 74 and 80%, respectively. No significant difference between groups was observed in clinical response rates (*P* values not reported).<br><br>Microbiological cure rates at test-of-cure assessment (seven to 14 days post-treatment) were 90% in the cefdinir QD group, 85% in the cefdinir BID group, and 88% in the cefuroxime group.<br><br>The cefdinir QD and BID groups were comparable to the cefuroxime group in microbiological cure rates at test-of-cure assessment but the cefdinir QD group was slightly more effective than the BID group (*P* values not reported).<br><br>At the long-term follow-up assessment (21 to 35 days post-treatment), the microbiological eradication rates were 95% for cefdinir QD, 99% for cefdinir BID and 99% for cefuroxime (*P* values not reported).<br><br>The corresponding values for clinical response rates were 93, 95 and 93%, respectively (*P* values not reported).<br><br>Secondary:<br>Thirty-two patients in the cefdinir QD group, 45 patients in the cefdinir BID group and 39 patients in the cefuroxime group developed a respiratory tract superinfection during the study (*P* values not reported).<br><br>Eleven patients were reinfected with pathogens not present at baseline after the test-of-cure assessment (three patients in the cefdinir QD group, six patients in the cefdinir BID group and two patients in the cefuroxime group; *P* values not reported). |
| Alvarez-Sala et al[30]<br><br>Cefuroxime 250 mg BID (for 10 days)<br><br>vs | DB, DD, PG, RCT<br><br>Patients 18 years of age and older with acute | N=541<br><br>5 to 10 days | Primary:<br>Clinical evaluation, bacteriologic evaluation<br><br>Secondary:<br>Adverse events | Primary:<br>On day 11, clinical success rate was reported as 79.9 and 82.7% for patients treated with cefditoren and cefuroxime, respectively (*P*=NS). On day 30, clinical success rate was reported as 81.0% and 85.5% for patients treated with cefditoren and cefuroxime, respectively (*P*=NS). On day 11, bacteriological response was reported as 72.8 and 67.0% for patients treated with cefditoren and cefuroxime, respectively (*P*=NS). |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
|---|---|---|---|---|
| cefditoren 200 mg BID (for 5 days) | exacerbations of chronic bronchitis | | | Secondary:<br>Drug-related adverse events were reported in 7.7 and 11.4% of patients treated with cefditoren and cefuroxime, respectively (*P* value not reported). |
| Zuck et al[31]<br><br>Cefuroxime 250 mg by mouth BID<br><br>vs<br><br>cefixime 200 mg BID | DB, MC, PG, RCT<br><br>Hospitalized patients 30 to 75 years of age experiencing acute exacer-bations of chronic bronchitis | N=58<br><br>8 days | Primary:<br>Clinical cure, microbiological eradication<br><br>Secondary:<br>Adverse events | Primary:<br>At two to four days post-treatment, clinical cure was reported in 94 and 71% of patients treated with cefuroxime and cefixime, respectively (*P*=NS); microbiological eradication occurred more quickly in patients treated with cefuroxime compared to patients treated with cefixime (*P*=0.002 at two to four weeks post-treatment).<br><br>Secondary:<br>Both treatments were well tolerated. One patient treated with cefuroxime reported fever; one patient treated with cefixime reported buccal mycosis. |
| Verghese et al[32]<br><br>Cephalexin 250 mg QID<br><br>vs<br><br>cefixime 400 mg for 1 dose | RCT<br><br>Patients with purulent exacerbation of chronic bronchitis | N=86<br><br>1 to 14 days | Primary:<br>Clinical cure, clinical improvement<br><br>Secondary:<br>Adverse events | Primary:<br>Clinical cure was reported as 70.8 and 50.0% in patients treated with cefixime and cephalexin, respectively (*P*<0.05). Combined percentages for clinical cure and improvement were reported as 95.8 and 84.2% in patients treated with cefixime and cephalexin, respectively (*P*=0.06).<br><br>Secondary:<br>Both treatments were well tolerated. Diarrhea occurred more often in patients treated with cefixime compared to patients treated with cephalexin (*P*=0.013). |
| Ziering et al[57]<br><br>Ceftibuten 400 mg QD<br><br>vs<br><br>clarithromycin 500 mg BID | DB, MC, PG<br><br>Patients 18 years of age and older with acute exacerbations of chronic bronchitis | N=309<br><br>7 to 14 days | Primary:<br>Clinical assessment, microbiological assessment, overall success rate<br><br>Secondary:<br>Adverse events | Primary:<br>At the end of the treatment, clinical success was reported in 91 and 93% of patients treated with ceftibuten and clarithromycin, respectively. At seven to 21 days post-treatment, clinical cure was reported as 92.6 and 93.3%, of patients treated with ceftibuten and clarithromycin, respectively. Overall success rate was reported as 84.3 and 86.7%, of patients treated with ceftibuten and clarithromycin, respectively (*P*=NS).<br><br>At the end of the treatment, microbiological eradication rates were reported in 84.8 and 89.5%, of patients treated with ceftibuten and clarithromycin, respectively. At seven to 21 days post-treatment, microbiological eradication was reported as 100% in both treatment groups (*P*=NS). |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
|---|---|---|---|---|
| | | | | Secondary:<br>Less patients treated with ceftibuten compared to clarithromycin reported drug-related adverse events (5.3 vs 21.9%, respectively; *P*<0.001) likely due to taste perversion associated with clarithromycin intake (*P*<0.001). |
| **Chancroid** | | | | |
| Martin et al[58]<br><br>Azithromycin 1 g as a single dose<br><br>vs<br><br>ceftriaxone 250 mg intramuscularly as a single dose | MC, RCT<br><br>Patients 16 years of age and older with the presence of a painful genital ulcer, negative darkfield examination, and a negative syphilis reagent test (unless the patient had a previous history of syphilis) | N=197<br><br>19 to 23 days | Primary:<br>Response to treatment<br><br>Secondary:<br>Not reported | Primary:<br>Complete healing was documented in 66% of azithromycin patients and 52% of ceftriaxone patients at the first visit (six to eight days after treatment; *P*>0.05).<br><br>By the third follow-up visit, 100% of patients in the azithromycin group were completely healed compared to 88% of patients in the ceftriaxone group (*P*>0.05). The remaining four patients in the ceftriaxone group at visit three were judged as clinically improved.<br><br>Secondary:<br>Not reported |
| **Female Pelvic and Genital Tract Infections** | | | | |
| French et al[59]<br><br>Clindamycin plus an aminoglycoside<br><br>vs<br><br>various alternative antibacterial regimens | MA<br><br>Women with postpartum endometritis, after cesarean section or vaginal birth | N=1,902<br><br>Precise duration of therapy not specified | Primary:<br>Treatment failure<br><br>Secondary:<br>Not reported | Primary:<br>Nineteen studies comparing clindamycin plus an aminoglycoside (usually gentamicin) with an alternative regimen demonstrated more treatment failures with the other regimen (RR, 1.44; 95% CI, 1.15 to 1.8).<br><br>The overall failure rate of clindamycin plus gentamicin was 11.4% (106/928).<br><br>The incidence of diarrhea was more common with the clindamycin regimens, though not at a statistically significant level (95% CI, 0.35 to 1.25).<br><br>Seven studies (N=741) compared a second or third generation cephalosporin with another regimen (usually clindamycin plus gentamicin) and demonstrated no difference in treatment failures between groups (RR,1.39; 95% CI, 0.90 to |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
|---|---|---|---|---|
| | | | | 2.15). The incidence of diarrhea was less frequent with the cephalosporin group.<br><br>Four trials (N=603) compared aztreonam plus clindamycin with other regimens (i.e., clindamycin plus gentamicin or trospectomycin) and did not reveal evidence of a difference between groups.<br><br>One trial (N=97) investigated the difference between ciprofloxacin and clindamycin plus gentamicin and demonstrated more treatment failures in the ciprofloxacin group, though not at a statistically significant level (RR,1.96; 95% CI, 0.20 to 4.21).<br><br>Secondary:<br>Not reported |
| **Gonorrhea** | | | | |
| Handsfield et al[33]<br><br>Cefixime 400 mg as a single dose<br><br>vs<br><br>cefixime 800 mg as a single dose<br><br>vs<br><br>ceftriaxone 250 mg intramuscularly as a single dose | RCT<br><br>Patients 16 years of age and older with isolation of *N gonorrhoeae* at enrollment | N=333<br><br>3 to 10 days post-treatment | Primary:<br>Cure rates<br><br>Secondary:<br>Not reported | Primary:<br>Overall cure rates were 96% in the cefixime 400 mg group, 98% in the cefixime 800 mg group and 98% in the ceftriaxone group (*P* values not reported).<br><br>Secondary:<br>Not reported |
| Verdon et al[34]<br><br>Cefixime 200 mg as a single dose | OL, RCT<br><br>Patients with gonococcal infection | N=125<br><br>4 to 7 days post-treatment | Primary:<br>Eradication rates<br><br>Secondary:<br>Not reported | Primary:<br>Genital and rectal gonorrhea was eradicated in 95% of patients.<br><br>Treatment was effective in 95% of men with urethral infection and 94% of women with anogenital infection.<br><br>Two of three pharyngeal infections were eradicated. |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
|---|---|---|---|---|
| | | | | Secondary:<br>Not reported |
| Plourde et al[35]<br><br>Cefixime 400 mg as a single dose<br><br>vs<br><br>ceftriaxone 250 mg intramuscularly as a single dose | RCT<br><br>Patients 18 to 65 years of age with *N gonorrhoeae* infection | N=236<br><br>4 to 7 days post-treatment | Primary:<br>Bacteriologic cure<br><br>Secondary:<br>Not reported | Primary:<br>Bacteriological cure was observed in 98% of cefixime patients and 100% of ceftriaxone patients (*P* value not reported).<br><br>Secondary:<br>Not reported |
| Portilla et al[36]<br><br>Cefixime 400 mg as a single dose<br><br>vs<br><br>cefixime 800 mg as a single dose<br><br>vs<br><br>ceftriaxone 250 mg intramuscularly as a single dose | RCT<br><br>Patients 18 to 44 years of age with gonococcal infection | N=187<br><br>4 to 9 days post-treatment | Primary:<br>Bacteriologic cure<br><br>Secondary:<br>Not reported | Primary:<br>Bacteriologic eradication was observed in 97% of cefixime patients and 100% of ceftriaxone patients.<br><br>Secondary:<br>Not reported |
| Novak et al[37]<br><br>Cefpodoxime 50 mg as a single dose<br><br>vs<br><br>cefpodoxime 100 mg as | DR, OL<br><br>Male patients 18 to 46 years of age with uncomplicated *N gonorrhoeae* infection | N=58<br><br>4 to 9 days post-therapy | Primary:<br>Eradication rates<br><br>Secondary:<br>Not reported | Primary:<br>A 100% eradication rate was observed at all dose groups from 50 to 600 mg. Among patients evaluated, eight β-lactamase positive strains were identified.<br><br>A dose of 200 mg of cefpodoxime was chosen for phase III studies due to efficacy and pharmacokinetic parameters.<br><br>Secondary: |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
|---|---|---|---|---|
| a single dose<br><br>vs<br><br>cefpodoxime 200 mg as a single dose<br><br>vs<br><br>cefpodoxime 400 mg as a single dose<br><br>vs<br><br>cefpodoxime 600 mg as a single dose<br><br>Doses started at 600 mg and were reduced when bacteriologic eradication rates were ≥90%.<br><br>When the eradication rate was ≤80% the dose was not reduced any further and the 10 previous subjects were to be given probenecid 1 g. | | | | Not reported |
| **Otitis Media** | | | | |
| Piippo et al[60]<br><br>Cefaclor 40 mg/kg/day divided BID<br><br>vs | DB, PG, RCT<br><br>Pediatric patients aged 6 months to 12 years with acute otitis media | N=345<br><br>7 days | Primary:<br>Clinical cure<br><br>Secondary:<br>Adverse events | Primary:<br>At days 10 to 12, clinical cure was reported in 93.5 and 90.5% of patients treated with cefixime and cefaclor, respectively (*P*=0.081). At days 28 to 35, clinical cure was reported in 90.1 and 86.6% of patients treated with cefixime and cefaclor, respectively (*P*=0.12).<br><br>Secondary: |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
|---|---|---|---|---|
| cefixime 8 mg/kg/day divided BID | | | | Adverse events were reported in 17.9 and 10.6% of patients treated with cefixime and cefaclor, respectively (*P* value not reported). |
| MacLoughlin et al[61]<br><br>Cefaclor suspension 40 mg/kg/day divided TID<br><br>vs<br><br>cefpodoxime suspension 10 mg/kg/day divided BID | MC, OL, RCT<br><br>Pediatric patients aged 1 month to 11 years with acute otitis media | N=167<br><br>5 days | Primary:<br>Clinical efficacy<br><br>Secondary:<br>Adverse events | Primary:<br>Clinical success was reported as 93.6 and 91.6% of patients treated with cefpodoxime and cefaclor, respectively (*P*>0.05); at study day 30, clinical recurrence was reported as 99 and 94%, respectively (*P*>0.05).<br><br>Secondary:<br>Patients were able to tolerate both cefpodoxime and cefaclor (99 vs 94%, respectively; *P*>0.05). |
| Blumer et al[62]<br><br>Cefaclor 40 mg/kg/day in 3 divided doses (maximum 1 g/day)<br><br>vs<br><br>ceftibuten 9 mg/kg/day for 1 dose (maximum 400 mg/day) | MC, RCT, SB<br><br>Pediatric patients aged 3 months to 17 years with acute otitis media | N=154<br><br>10 days | Primary:<br>Clinical cure<br><br>Secondary:<br>Adverse events | Primary:<br>At one to three days post-treatment, clinical cure was reported in 89 and 88% of patients treated with ceftibuten and cefaclor, respectively (*P*=NS). At two to four weeks post-treatment, clinical cure was reported in 88 and 82% of patients treated with ceftibuten and cefaclor, respectively (*P*=NS).<br><br>Secondary:<br>Mild to moderate drug-related adverse events were reported in 8 and 14% of patients treated with ceftibuten and cefaclor, respectively (*P* values not reported). |
| Block et al[63]<br><br>Cefprozil 30 mg/kg/day divided BID (for 10 days)<br><br>vs<br><br>cefdinir 14 mg/kg/day divided BID (for 5 days) | DB, MC, PRO<br><br>Pediatric patients aged 6 months to 12 years with acute otitis media | N=373<br><br>5 to 10 days | Primary:<br>Clinical cure<br><br>Secondary:<br>Adverse events | Primary:<br>At the end of therapy (study days nine to 11), clinical efficacy was reported as 80.0 and 82.5% in patients treated with cefdinir and cefprozil (*P*=NS).<br><br>Secondary:<br>Diarrhea and overall adverse events were reported in cefdinir-treated patients (7.8 and 13.0%, respectively) and cefprozil-treated patients (4.2 and 12.0%, respectively; *P*=0.116). |
| Asmar et al[38]<br><br>Cefixime oral suspension 8 mg/kg/day QD | DB, MC, PRO, RCT<br><br>Patients aged 2 months to 17 | N=368<br><br>10 days | Primary:<br>Clinical evaluations, microbiologic evaluations | Primary:<br>On days 12 through 15, clinical cure or improvement was reported in 83 and 81% of patients treated with cefpodoxime and cefixime, respectively (*P*=0.541).<br><br>On days 12 to 15, end-of-therapy response rates were reported as 53 and 51% |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
|---|---|---|---|---|
| vs<br><br>cefpodoxime oral suspension 10 mg/kg/day QD | years with acute suppurative otitis media | | Secondary:<br>Adverse events | in patients treated with cefpodoxime and cefixime, respectively (*P*=0.404).<br><br>Overall microbiologic susceptibility was reported as 89 and 86% in patients treated with cefpodoxime and cefixime, respectively (*P*=0.70).<br><br>Secondary:<br>Drug-related adverse effects (e.g., diarrhea, diaper rash, vomiting and rash) occurred in 23.3 and 17.9% of patients treated with cefpodoxime and cefixime, respectively (no *P* values reported). |
| Block et al[64]<br><br>Azithromycin suspension 10 mg/kg QD on day 1 then 5 mg/kg QD for 4 days<br><br>vs<br><br>cefdinir suspension 7 mg/kg every 12 hours for 5 days | MC, PRO, RCT, SB<br><br>Patients 6 months to 6 years of age with acute otitis media | N=357<br><br>25 days | Primary:<br>Clinical response, signs and symptoms of infection<br><br>Secondary:<br>Parental satisfaction with treatment, adverse events | Primary:<br>Clinical cure rates at the end-of-therapy visit (seven to nine days) were comparable between groups (85% for azithromycin and 87% for cefdinir; 95% CI, -5.5 to 9.8).<br><br>Comparable clinical cure rates were sustained at the follow-up visit (20 to 25 days) in patients who were cured at the end-of-therapy visit (86% for azithromycin and 76% for cefdinir; 95% CI, -18.9 to 0.0).<br><br>Clinical cure rates at end-of-therapy were comparable between groups in patients who were previously vaccinated with conjugated heptavalent pneumococcal vaccine (PCV7) 83% for azithromycin and 86% for cefdinir; 95% CI, -6.5 to 11.8).<br><br>No significant differences were observed between groups in signs and symptoms of infection at the end-of-therapy visit.<br><br>Secondary:<br>The study drugs were comparable based on parental satisfaction ratings, ease of use, taste, compliance, health care resource utilization and missed work or daycare.<br><br>Most adverse events were mild or moderate and resolved without need for additional treatment. |
| Mandel et al[65]<br><br>Erythromycin/ | DB, RCT<br><br>Patients 7 | N=331<br><br>12 weeks | Primary:<br>Proportion of patients effusion- | Primary:<br>There were no significant differences in the proportion of patients who were effusion-free in the erythromycin/sulfisoxazole or cefaclor group compared to the |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
|---|---|---|---|---|
| sulfisoxazole 50 mg/kg/day of erythromycin component and 150 mg/kg/day of sulfisoxazole component in four divided doses<br><br>vs<br><br>amoxicillin 40 mg/kg/day in three divided doses<br><br>vs<br><br>cefaclor 40 mg/kg/day in 3 divided doses<br><br>vs<br><br>placebo | months to 12 years of age with otitis media with effusion and without symptoms of acute otitis media (otalgia, fever) | | free at two and four weeks in the erythromycin/ sulfisoxazole and cefaclor groups compared to the amoxicillin group<br><br>Secondary:<br>Recurrence rate of middle ear effusion following antibiotic therapy, speech recognition threshold at two and four weeks | amoxicillin group at week two or four ($P \geq 0.39$).<br><br>Secondary:<br>There were no significant differences between groups in the recurrence rate of middle ear effusion after antibiotic therapy.<br><br>Speech recognition threshold was statistically higher in both the right and left ears in the placebo group than in the antimicrobial groups at two weeks ($P \leq 0.04$).<br><br>At four weeks, this difference was only present in the right ear ($P=0.03$), not in the left ear ($P=0.19$). |
| Casey et al[66]<br><br>Cefdinir 14 mg/kg/day divided twice daily for five days<br><br>vs<br><br>amoxicillin/clavulanic acid 80 mg/kg/day (of amoxicillin) divided twice daily for 10 days | MC, RCT<br><br>Patietns six to 24 months of age with acute otitis media | N=330<br><br>5 to 10 days | Primary:<br>Clincal cure<br><br>Secondary:<br>Not reported | Primary:<br>The clinical cure rate with amoxicillin/clavulanic acid high dose (86.5%) was significantly higher than that with cefdinir (71.0%; P=0.001).<br><br>There is a significant difference between the two antibiotics according to the age of the child (P<0.002). The difference in efficacy with high-dose amoxicillin/clavulanic acid between the ages of 6 and 24 months in the children treated did not impact the overall cure rate (OR, 0.87; 95% CI, 0.28 to 2.69; P=0.8). In contrast, the difference in efficacy with cefdinir between the ages of 6 and 24 months in the children treated did adversely impact the overall cure rate (OR, 0.28; 95% CI, 0.10 to 0.78; P=0.01). |
| **Pharyngitis/Tonsillitis** | | | | |
| Nemeth et al[39] | DB, MC, RCT | N=919 | Primary:<br>Clinical response, | Primary:<br>At the test-of-cure visit (four to nine days post-treatment), clinical cure rates for |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
|---|---|---|---|---|
| Cefdinir 600 mg QD<br><br>vs<br><br>cefdinir 300 mg BID<br><br>vs<br><br>penicillin V 250 mg QID | Patients 13 years of age and older with erythema and pain of the pharyngeal cavity and a positive rapid streptococcal antigen test | Up to 24 days post-therapy | microbiological response<br><br>Secondary:<br>Tolerability | the cefdinir QD, cefdinir BID and penicillin groups were 94.8, 96.3 and 88.9% respectively (*P*=0.02 for penicillin compared to cefdinir QD and *P*<0.01 for penicillin compared to cefdinir BID).<br><br>At the test-of-cure visit (four to nine days post-treatment), microbiological cure rates for the cefdinir QD, cefdinir BID and penicillin groups were 91.4, 91.7 and 83.4% respectively (*P*=0.02 for penicillin compared to cefdinir QD and *P*=0.01 for penicillin compared to cefdinir BID).<br><br>No significant differences were observed in clinical or microbiological cure rates between cefdinir QD and cefdinir BID groups (*P*=0.52 and *P*=0.95 respectively).<br><br>At long-term follow-up (17 to 24 days post-treatment), microbiological eradication rates were 94.9, 96.1 and 92.3% respectively for cefdinir QD, cefdinir BID and penicillin (*P* values not reported).<br><br>At long-term follow-up (17 to 24 days post-treatment), clinical cure rates were 95.6, 98.4 and 92.8% respectively for cefdinir QD, cefdinir BID and penicillin (*P* values not reported).<br><br>Secondary:<br>Significantly more adverse effects were observed in the cefdinir groups compared to the penicillin group (*P*<0.001). |
| Tack et al[40]<br><br>Cefdinir 300 mg BID<br><br>vs<br><br>penicillin V 250 mg QID | MC, RCT, SB<br><br>Patients 13 years of age and older with erythema and pain of the pharyngeal cavity and a positive rapid streptococcal antigen test | N=558<br><br>Up to 31 days | Primary:<br>Clinical response, microbiological response<br><br>Secondary:<br>Not reported | Primary:<br>The clinical cure rates at test-of-cure (five to 10 days post-therapy) were 89.0 and 84.6% in the cefdinir and penicillin groups respectively (95% CI for difference in cure rates, -2.0 to 10.8).<br><br>The microbiological eradication rates at test-of-cure (five to 10 days post-therapy) were 88.5 and 82.2% in the cefdinir and penicillin groups respectively (95% CI for difference in eradication rates, -0.4 to 12.9).<br><br>At long-term follow-up, eradication rates were 81.7 and 77.9% for the cefdinir and penicillin groups respectively.<br><br>Secondary: |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
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| | | | | Not reported |
| Brook[41]<br><br>Cefdinir 600 mg (adults) or 14 mg/kg (pediatrics) QD (for 10 days)<br><br>vs<br><br>cefdinir 300 mg (adults) or 7 mg/kg (pediatrics) BID (for 5 to 10 days)<br><br>vs<br><br>penicillin 250 mg (adults) or 10 mg/kg (pediatrics) QID (for 10 days)<br><br>In studies A through D, participants received either cefdinir or penicillin. | 4 DB/SB, MC, PC, RCT<br><br>Patients with throat pain, erythema, and a positive rapid streptococcal screening test; study A and B participants were <13 years of age; study C and D participants were ≥13 years of age | N=2,751<br><br>5 to 10 days | Primary:<br>Clinical cure rate, bacterial eradication rate<br><br>Secondary:<br>Adverse events | Primary:<br>Combined clinical cure rate was reported as higher for patients treated with cefdinir compared to patients treated with penicillin (94 vs 83%, respectively; *P*<0.001). Combined bacterial eradication rate was higher for patients treated with cefdinir compared to patients treated with penicillin (92 vs 77%, respectively; *P*<0.001).<br><br>Secondary:<br>All treatments were well tolerated; 98% of patients completed the treatment regimens. Patients treated with cefdinir reported diarrhea, nausea, headache, and vaginal moniliasis; patients treated with penicillin reported diarrhea, nausea, headache, and vomiting. |
| Ozaki et al[42]<br><br>Cefditoren 3 mg/kg TID<br><br>vs<br><br>amoxicillin 10 mg/kg TID | PRO<br><br>Pediatric patients with group A streptococcal pharyngitis | N=258<br><br>4 weeks | Primary:<br>Eradication rates, recurrence rates<br><br>Secondary:<br>Not reported | Primary:<br>Eradication was observed in 99% of cefditoren patients and 100% of amoxicillin patients. No significant differences were observed between groups in eradication rates (*P*=0.22).<br><br>Recurrence occurred in eight and 15 patients in the cefditoren and amoxicillin groups respectively. No significant differences were observed between groups in recurrent rates (*P*=0.61).<br><br>Secondary:<br>Not reported |
| Block et al[43] | OL, RCT | N=110 | Primary:<br>Clinical response, | Primary:<br>No significant difference was observed between the cefixime and penicillin |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
|---|---|---|---|---|
| Cefixime 8 mg/kg QD<br><br>vs<br><br>penicillin V 250 mg TID | Pediatric patients 4 to 12 years of age with group A β-hemolytic streptococcal pharyngitis | 6 weeks | bacteriological response<br><br>Secondary:<br>Not reported | groups in clinical cure at the end of treatment (two to seven days post-treatment; *P* value not reported).<br><br>Significantly more patients in the penicillin group experienced a relapse compared to those in the cefixime group (11 and three respectively; *P*<0.05).<br><br>At the end of treatment, eradication rates were significantly higher in the cefixime group compared to the penicillin group (94 and 77% respectively; *P*<0.05).<br><br>Up to six weeks post-therapy, significantly more patients in the penicillin group had positive group A β-hemolytic streptococcus cultures compared to patients in the cefixime group (45 and 21% respectively; *P*<0.05).<br><br>Secondary:<br>Not reported |
| Adam et al[44]<br><br>Cefixime 8 mg/kg QD<br><br>vs<br><br>penicillin V 20,000 units/kg TID | OL, RCT<br><br>Pediatric patients 1 to 12 years of age with pharyngitis and/or tonsillitis | N=160<br><br>4 weeks post-therapy | Primary:<br>Clinical response, bacteriological response<br><br>Secondary:<br>Safety and tolerability | Primary:<br>The clinical response rate was 96.0% in the cefixime group and 97.4% in the penicillin group (*P* value not reported).<br><br>Eradication rates were 82.6 and 88.2% in the cefixime and penicillin group respectively (*P* value not reported).<br><br>Recurrence at three to four weeks post-therapy was 8.0% in the cefixime group and 10.5% in the penicillin group (*P* value not reported).<br><br>Secondary:<br>Both medications were well-tolerated. Adverse events were observed in four children (5.0%) in the cefixime group and five patients (6.3%) in the penicillin group (*P* value not reported). |
| Pichichero et al[45]<br><br>Cefpodoxime suspension 10 mg/kg/day divided in 2 doses (for 5 days; maximum of 200 mg/day) | DB, MC, PRO, RCT'<br><br>Patients aged 2 to 17 years with acute tonsillo-pharyngitis | N=484<br><br>5 to 10 days | Primary:<br>Clinical efficacy, bacteriologic efficacy<br><br>Secondary:<br>Adverse events | Primary:<br>Clinical efficacy was reported as 96, 94, and 91% for patients treated with cefpodoxime (10 days), cefpodoxime (five days), and penicillin, respectively (*P*=NS). At study days five to 10, bacteriologic eradication rates were reported as 95, 90, and 78% for patients treated with cefpodoxime (10 days), cefpodoxime (five days), and penicillin, respectively (*P*=0.003 and *P*=0.02 for cefpodoxime [10 days] and cefpodoxime [five days] vs penicillin, respectively). |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
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| vs<br><br>cefpodoxime suspension 10 mg/kg/day as 1 dose (for 10 days; maximum of 200 mg/day)<br><br>vs<br><br>penicillin suspension 40 mg/kg/day divided into 3 doses (for 10 days; maximum 1 g/day) | | | | By the 32- to 38-day post treatment visit, cumulative bacteriologic failure rate was reported as 17, 19, and 35% for patients treated with cefpodoxime (10 days), cefpodoxime (five days), and penicillin, respectively (*P*=0.001 and *P*=0.005 for cefpodoxime [10 days] and cefpodoxime [five days] vs penicillin, respectively).<br><br>Secondary:<br>All treatments were well-tolerated. Gastrointestinal symptoms were most commonly reported. |
| Pichichero et al[46]<br><br>Ceftibuten 9 mg/kg QD<br><br>vs<br><br>penicillin 25 mg/kg/day in 3 divided doses | MC, RCT, SB<br><br>Patients 3 to 18 years of age with pharyngitis and scarlet fever caused by group A β-hemolytic streptococci | N=617<br><br>5 to 7 days post-treatment (primary endpoint) and up to 4 weeks follow-up | Primary:<br>Clinical response, bacteriological response<br><br>Secondary:<br>Not reported | Primary:<br>Significantly more patients in the ceftibuten group achieved clinical cure or improvement compared to patients in the penicillin group at five to seven days post-treatment (97 and 89% respectively; *P*<0.01).<br><br>At two to three weeks post-treatment, clinically successful outcomes were comparable between patients in the ceftibuten and penicillin groups (90 and 89% respectively; *P* value not reported).<br><br>Strains producing scarlet fever responded in a comparable manner to both ceftibuten and penicillin.<br><br>Significantly more patients in the ceftibuten group achieved bacteriologic elimination compared to patients in the penicillin group at five to seven days post-treatment (91 and 80% respectively; *P*<0.01).<br><br>Higher bacteriological eradication rates were observed in ceftibuten patients with pharyngitis (91%) or scarlet fever (90%) compared to penicillin patients with pharyngitis (80%) or scarlet fever (71%) (*P* values not reported).<br><br>At two to three weeks post-treatment, no significant differences were observed between the ceftibuten and penicillin groups in bacteriological eradication rates (89 and 79% respectively; *P* value not reported). |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
|---|---|---|---|---|
| | | | | Secondary:<br>Not reported |
| **Pneumonia/Lower Respiratory Tract Infections** | | | | |
| van Zyle L et al[47]<br><br>Cefditoren 200 mg BID<br><br>vs<br><br>cefditoren 400 mg BID<br><br>vs<br><br>cefpodoxime 200 mg BID | DB, MC, PRO, RCT<br><br>Patients 12 years of age and older with community-acquired pneumonia | N=851<br><br>7 to 14 days post-treatment | Primary:<br>Clinical response, microbiological response<br><br>Secondary:<br>Not reported | Primary:<br>Clinical cure rates were similar between groups at both the post-treatment (48 hours post-treatment) and follow-up visits (seven to 14 days post-treatment).<br><br>The overall clinical cure rates for cefditoren 200 mg, cefditoren 400 mg and cefpodoxime were 90.5, 89.7 and 92.2% respectively at the post-treatment visit and 88.4, 87.2 and 90.4% respectively at the follow-up visit (*P* values not reported).<br><br>At the post-treatment visit, the overall eradication rates were 88.7% for cefditoren 200 mg, 89.9% for cefditoren 400 mg and 95.7% for cefpodoxime. A significantly better eradication rate was observed for cefpodoxime compared to cefditoren 200 mg (*P*=0.031).<br><br>At the follow-up visit, the overall eradication rates were 80.0% for cefditoren 200 mg, 85.7% for cefditoren 400 mg and 91.7% for cefpodoxime. A significantly better eradication rate was observed for cefpodoxime compared to cefditoren 200 mg (*P*=0.005).<br><br>Secondary:<br>Not reported |
| Drehobl et al[48]<br><br>Cefaclor 500 mg TID<br><br>vs<br><br>cefdinir 300 mg BID | DB, MC, RCT<br><br>Patients with community-acquired pneumonia | N=538<br><br>10 days | Primary:<br>Clinical response, microbiological eradication<br><br>Secondary:<br>Adverse events | Primary:<br>Satisfactory clinical response was reported as 89 and 86% of patients treated with cefdinir and cefaclor, respectively; microbiological eradication was reported as 92 and 93%, respectively (*P*=NS).<br><br>Secondary:<br>Patients treated with cefdinir reported a higher incidence of diarrhea compared to patients treated with cefaclor (13.7 vs 5.3%, respectively; *P*<0.001). |
| Sengupta et al[49]<br><br>Cefixime 4 mg/kg BID | AC, MC, OL, PRO, RCT | N=776<br><br>10 to 14 days | Primary:<br>Clinical cure, bacteriologic | Primary:<br>Clinical cure was reported as 97.0 and 86.8% for patients treated with cefpodoxime and cefixime, respectively; bacteriologic eradication was reported |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
|---|---|---|---|---|
| vs<br><br>cefpodoxime 5 mg/kg BID | Pediatric patients aged 6 months to 12 years with community-acquired lower respiratory tract infections, including community-acquired pneumonia and acute exacerbations of chronic bronchitis | | eradication<br><br>Secondary:<br>Adverse events | as 93.4 and 82.9%, respectively (no *P* values were reported).<br><br>Secondary:<br>Both treatments were well tolerated. |
| **Skin and Soft Tissue Infections** | | | | |
| Tack et al[50]<br><br>Cephalexin 10 mg/kg QID<br><br>vs<br><br>cefdinir 7 mg/kg BID | DB, MC, RCT<br><br>Patients 6 months to 12 years of age diagnosed with an uncomplicated mild to moderate skin or skin-structure infection warranting systemic anti-microbial therapy and/or drainage | N=231<br><br>10 days | Primary:<br>Clinical cure rate, microbiologic eradication rate<br><br>Secondary:<br>Adverse events | Primary:<br>Clinical cure rates were reported as 98.3 and 93.8% in patients treated with cefdinir and cephalexin, respectively (*P*=0.056). Microbiologic eradication rates were reported as 99.4 and 97.4% in patients treated with cefdinir and cephalexin, respectively (*P*=0.14).<br><br>Secondary:<br>Drug-related adverse events were reported in 16 and 11% of patients treated with cefdinir and cephalexin, respectively (*P*=0.11). The most common side effect was diarrhea. |
| Tack et al[51] | DB, MC, RCT | N=382 | Primary:<br>Pathogen | Primary:<br>No significant difference was observed between groups in pathogen eradication |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
|---|---|---|---|---|
| Cephalexin 500 mg QID for 10 days<br><br>vs<br><br>cefdinir 300 mg BID for 10 days | Patients 13 years of age and older with acute skin and skin structure infections | 7 to 16 days post-therapy | eradication rate, clinical success rate<br><br>Secondary:<br>Not reported | rate (93% for cefdinir and 89% for cephalexin; *P*=0.105).<br><br>No significant difference was observed in the rate of superinfection between groups (*P*=0.22).<br><br>No significant differences between groups was observed in clinical success rates (88% for cefdinir and 87% for cephalexin; *P*=0.617).<br><br>Secondary:<br>Not reported |
| Stevens et al[52]<br><br>Cefaclor 500 mg TID<br><br>vs<br><br>cefpodoxime 400 mg BID<br><br>vs<br><br>placebo BID to TID | DB, MC, PC, RCT<br><br>Patients 12 years of age and older with acute single-site skin or skin-structure infections | N=371<br><br>7 to 10 days | Primary:<br>Clinical efficacy and safety<br><br>Secondary;<br>Not reported | Primary:<br>High pathogen eradication rates were observed for patients treated with either cefaclor or cefpodoxime (98 vs 99%, respectively; *P* value not reported). Patients with infected wounds responded better to cefpodoxime compared to cefaclor (100 vs 83%, respectively; *P* value not reported). Patients treated with cefaclor reported a higher failure rate compared to patients treated with cefpodoxime (4 vs 1%, respectively; *P*=NS). Both active drug regimens were well tolerated.<br><br>Secondary:<br>Not reported |
| Bucko et al[53]<br><br>Cefadroxil 500 mg BID<br><br>vs<br><br>cefditoren 200 mg BID<br><br>vs<br><br>cefditoren 400 mg BID<br><br>vs<br><br>cefuroxime 250 mg BID | MA (2 DB, MC, PG)<br><br>Patients with uncomplicated skin and skin structure infections | N=1,685<br><br>10 days | Primary:<br>Clinical evaluation, microbiologic evaluation<br><br>Secondary:<br>Adverse events | Primary:<br>Clinical cure rates were reported as 85, 83, 88 and 85% for patients treated with cefditoren 200 mg, cefditoren 400 mg, cefuroxime, and cefadroxil, respectively (no *P* values reported).<br><br>At seven to 14 days after treatment completion, eradication rates were higher in patients treated with cefuroxime compared to patients treated with cefditoren 200 mg in study one (*P*=0.043). At seven to 14 days after treatment completion, eradication rates were higher for cefditoren 400 mg compared to patients treated with cefadroxil in study two (*P*=0.018).<br><br>Secondary:<br>A higher rate of drug-related adverse events were reported for patients treated with cefditoren 400 mg compared to all other treatment groups (*P*<0.05 for each comparison). The most common adverse events were mild cases of diarrhea, |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
|---|---|---|---|---|
| In study A, participants received cefditoren 200 mg or cefuroxime; in study B, participants received cefditoren 400 mg or cefadroxil. | | | | nausea, and headache. |
| **Sinusitis** | | | | |
| Gehanno et al[54]<br><br>Cefaclor 500 mg TID<br><br>vs<br><br>cefpodoxime 200 mg BID | DB, MC, PC, PRO, RCT<br><br>Adult outpatients with acute sinusitis | N=236<br><br>Mean days 9.9 | Primary:<br>Clinical cure, overall clinical efficacy (cure and improvement), bacteriological eradication<br><br>Secondary:<br>Adverse events | Primary:<br>At the end of the treatment, clinical cure was reported as 84 and 68% of patients treated with cefpodoxime and cefaclor, respectively (*P*=0.01). Overall clinical efficacy was reported as 95 and 93% of patients treated with cefpodoxime and cefaclor, respectively (*P*=NS). Bacteriological eradication was reported as 95 and 91% of patients treated with cefpodoxime and cefaclor, respectively (*P*=NS).<br><br>Secondary:<br>Possible drug-related adverse events were reported in nine and 10 patients treated with cefpodoxime and cefaclor, respectively; *P* value not reported. |
| **Surgical Prophylaxis** | | | | |
| Song et al[67]<br><br>Cefuroxime plus metronidazole<br><br>vs<br><br>gentamicin plus metronidazole<br><br>vs<br><br>first generation or second generation cephalosporin<br><br>vs | MA<br><br>MA of 147 relevant RCTs published between 1984 and 1995 | 147 trials<br><br>12 years | Primary:<br>Rate of surgical wound infections<br><br>Secondary:<br>Not reported | Primary:<br>There was no significant difference in the rate of surgical wound infections between many different regimens.<br><br>However, certain regimens appeared to be inadequate (e.g., metronidazole alone, doxycycline alone, piperacillin alone, oral neomycin plus erythromycin on the day before operation).<br><br>A single dose administered immediately before the operation (or short-term use) was judged as effective as long-term postoperative antimicrobial prophylaxis (OR, 1.17; 95% CI, 0.90 to 1.53).<br><br>There is no convincing evidence to suggest that the new-generation cephalosporins are more effective than first generation cephalosporins (OR, 1.07; 95% CI, 0.54 to 2.12).<br><br>Secondary: |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
|---|---|---|---|---|
| third generation cephalosporin<br><br>vs<br><br>other antibiotic agents as mono or combination therapy | | | | Not reported |
| **Urinary Tract Infections** | | | | |
| Leigh et al[55]<br><br>Cefaclor 250 mg TID<br><br>vs<br><br>cefdinir 100 mg BID | DB, MC, PG, RCT<br><br>Patients 13 years of age and older with uncomplicated urinary tract infections | N=383<br><br>5 days | Primary:<br>Clinical and microbiologic efficacy<br><br>Secondary:<br>Adverse events | Primary:<br>A greater number of pathogens were resistant to treatment with cefaclor compared to treatment with cefdinir (6.7 vs 3.7%, respectively; *P*<0.003). Isolates of *E coli* were more resistant to treatment with cefaclor compared to treatment with cefdinir (5.1 vs 2.0%, respectively; *P*<0.007).<br><br>At five to nine days post treatment, patients treated with cefdinir and cefaclor reported statistically equivalent clinical (91.3 vs 93.0%, respectively; *P*=0.539) and microbiologic (84.7 vs 79.7%, respectively; *P*=0.184) response rates.<br><br>Secondary:<br>Drug-related side effects were greater in patients treated with cefdinir compared to patients treated with cefaclor (20.2 vs 13.0%, respectively; *P*=0.025). |
| Ho et al[56]<br><br>Cefixime 200 mg BID<br><br>vs<br><br>ceftibuten 200 mg BID | OL, PRO, RCT<br><br>Patients 18 years of age and older with complicated urinary tract infections | N=45<br><br>10 to 14 days | Primary:<br>Clinical efficacy rate, bacteriological eradication rate<br><br>Secondary:<br>Adverse events | Primary:<br>There was no statistically significant difference in rates of clinical efficacy (78.3 vs 77.3%; *P*=0.9) and bacteriological eradication (52.2 and 63.6%; *P*=0.08) for patients taking ceftibuten and cefixime, respectively.<br><br>Secondary:<br>Adverse events were minimal for both treatment groups. Patients treated with ceftibuten reported diarrhea and increased transaminase serum levels; patients treated with cefixime reported skin rash and increased transaminase serum levels. |
| Zalmanovici Trestioreanu et al[68]<br><br>Nitrofurantoin | MA<br><br>Outpatient women 16 to 65 | N=6,016<br><br>≥3 days | Primary:<br>Short-term symptomatic cure and long-term | Primary:<br>There was no statistically significant difference in short-term and long-term symptomatic cure with any of the treatment comparisons: fluoroquinolones vs SMX/TMP (RR, 1.00; 95% CI, 0.97 to 1.03; *P*=0.89 and RR, 0.99; 95% CI, 0.94 |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
|---|---|---|---|---|
| vs<br><br>SMX/TMP<br><br>vs<br><br>β-lactams (amoxicillin, cefadroxil, cefpodoxime pivmecillinam*)<br><br>vs<br><br>nalidixic acid<br><br>vs<br><br>fluoroquinolones (amifloxacin*, ciprofloxacin, norfloxacin, ofloxacin) | years of age with uncomplicated UTI defined by the presence of urinary complaints (and the absence of upper UTI signs) and leucocyturia or bacteriuria | | symptomatic cure<br><br>Secondary:<br>Short-term bacteriological cure, long-term bacterial cure, proportion of patients that developed resistance ≤8 weeks after treatment period, numbers of days to symptom resolution, days of work-loss, adverse event resulting in discontinuation of therapy, proportion of patients that developed rash, diarrhea, any adverse event or complications | to 1.05), β-lactams vs SMX/TMP (RR, 0.95; 95% CI, 0.81 to 1.39; *P*=0.56 and RR, 1.06; 95% CI, 0.93 to 1.21; *P*=0.40), nitrofurantoin vs β-lactams (RR, 1.19; 95% CI, 0.93 to 1.51 and RR, 0.98; 95% CI, 0.83 to 1.14), fluoroquinolones vs β-lactams (RR, 1.15; 95% CI, 0.99 to 1.32; *P*=0.064 and RR, 1.01; 95% CI, 0.96 to 1.05) and nitrofurantoin vs SMX/TMP (RR, 0.99; 95% CI, 0.95 to 1.04; *P*=0.82 and RR, 1.01; 95% CI, 0.94 to 1.09; *P*=0.81).<br><br>Secondary:<br>In the ITT population comparing fluoroquinolones and SMX/TMP, there was a significant difference in short-term bacteriologic cure that slightly favored fluoroquinolones (RR, 1.03; 95% CI, 1.00 to 1.07; *P*=0.025). The result was no longer significant when patients with susceptible pathogens were compared (RR, 1.03; 95% CI, 0.98 to 1.07; *P*=0.23). This result was similar for long-term bacteriologic cure comparing fluoroquinolones and SMX/TMP (RR, 1.06; 95% CI, 1.00 to 1.12; *P*=0.046). When comparing fluoroquinolones vs β-lactams, short-term bacteriologic cure was significantly greater in patients treated with fluoroquinolones in the ITT population (RR, 1.22; 95% CI, 1.13 to 1.31; *P*<0.00001) and the patients with susceptible pathogens (RR, 1.20; 95% CI 1.07 to 1.35; *P*=0.0018). There were no significant differences in short-term and long-term bacteriologic cure comparing the other treatment groups.<br><br>Significantly less patients developed rashes with fluoroquinolones vs SMX/TMP (RR, 0.08; 95% CI, 0.71 to 1.29; *P*=0.0.0035) or β-lactams (RR, 0.10; 95% CI, 0.02 to 0.56; *P*=0.0083) and with nitrofurantoin vs SMX/TMP (RR, 0.17; 95% CI, 0.04 to 0.76; *P*=0.020). There were no significant differences in rashes comparing the other treatment groups.<br><br>Data either could not be analyzed or was missing for number of days to symptom resolution or days of work loss. There were no significant differences in any of the other secondary outcomes when comparing treatment groups. |
| Bocquet et al[69]<br><br>Cefixime 8 mg/kg initially followed by 4 mg/kg BID for 10 days | AC, DB, MC, PRO, RCT<br><br>Infants and children aged 1 to 36 months | N=171<br><br>10 days | Primary:<br>Incidence of renal scarring<br><br>Secondary:<br>Time to apyrexia, | Primary:<br>In the intent-to-treat population, the incidence of renal scarring was 41% (95% CI, 28.7 to 53.3) for children in the oral cefixime alone treatment group and 44.8% (95% CI, 32.0 to 57.6) in the sequential treatment group (difference, -3.8%; 95% CI, -21.6 to 13.9). |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
|---|---|---|---|---|
| vs<br><br>ceftriaxone 50 mg/kg IV QD for 4 days followed by cefixime 4 mg/kg BID for 6 days | who presented to an emergency department with a first febrile UTI (defined as fever of ≥38.5° C) with no alternative source for the fever and positive urinalysis (white cell counts ≥$10^5$/mL) and gram-negative rods in gram-stained urine | | adverse events, serum procalcitonin and vesicoureteral reflux | In the per-protocol analysis, the frequency of renal scarring was 30.8% (95% CI, 18.3 to 43.3) in the oral cefixime treatment group and 27.3% (95% CI, 14.1 to 40.5) for the sequential treatment group (difference, 3.5%; 95% CI, -14.7 to 21.7).<br><br>In the per-protocol analysis, the incidence of scarring did not differ in between children younger than one year of age and children one to three years of age. The incidence of scarring also did not differ with respect to gender. In the subgroup of children less than three months of age (N=10), there were no infants with renal scarring in the cefixime oral group and two infants with renal scarring in the sequential treatment group.<br><br>Secondary:<br>The time to apyrexia was no different between the two treatment groups (median, 24 hours in both groups).<br><br>Two children did not tolerate cefixime because of vomiting, and treatment was changed to parenteral therapy. One child with apparent sepsis received intravenous ceftriaxone instead of oral cefixime.<br><br>The mean serum procalcitonin concentration was higher in children with renal scarring than in children without scarring (3.2 vs 1.7 ng/mL; *P*=0.002).<br><br>Voiding cystography was performed for 152 children, of which 40 were found to have vesicoureteral reflux (26.3%). Renal scarring was similar for children with or without vesicoureteral reflux. |
| Hooton et al[70]<br><br>Cefpodoxime 100 mg BID for 3 days<br><br>vs<br><br>ciprofloxacin 250 mg BID for 3 days | AC, DB, NI, RCT<br><br>Women 18 to 55 years of age with acute cystitis (symptoms of dysuria, frequency, | N=300<br><br>30 days | Primary:<br>Clinical cure rate at day 30<br><br>Secondary:<br>Clinical and microbiological cure at the first follow-up visit and vaginal *E. coli* colonization at | Primary:<br>The overall clinical cure rate at 30 days was 93% for women treated with ciprofloxacin compared to 82% of the cefpodoxime group (difference, 11%; 95% CI, 3 to 18). Because the upper limit of the 95% confidence interval of the difference exceeded 10%, the results did not meet predefined criteria for noninferiority of cefpodoxime (*P*=0.57).<br><br>Among women without a UTI in the year prior to enrollment, the 30-day clinical cure rate was 96% for the ciprofloxacin group compared to 83% of women treated with cefpodoxime (difference, 13%; 95% CI, 5 to 21). This difference was |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
|---|---|---|---|---|
| | and/or urgency) and pyuria (white blood cell count≥8 cells/$mm^3$), and received antimicrobial treatment and also had a positive urine culture (defined as 102 or more colony-forming units/mL of uropathogen). | | each follow-up visit | not seen among women who reported one or more UTIs in the year before enrollment (84 vs 80%, respectively).<br><br>Among women infected with strains that were susceptible to the study antibiotics, the overall clinical cure rates were 94% for ciprofloxacin compared to 82% for cefpodoxime (difference, 12%; 95% CI, 4 to 20). Among those infected with strains unsusceptible to the treatment antibiotic, the overall clinical cure rate was 50% in the ciprofloxacin group and 67% for cefpodoxime.<br><br>Secondary:<br>The clinical cure rate at the first follow- up visit (five days following treatment) was 93% for ciprofloxacin compared to 88% for cefpodoxime (difference, 5%; 95% CI, -1 to 12).<br><br>Among patients with available urine culture data, *E. coli* was the causative organism in 38% of nonresponders to treatment for ciprofloxacin compared to 64% for cefpodoxime.<br><br>Thirteen of 16 women in the cefpodoxime group with no response to treatment caused by *E. coli* had cefpodoxime-susceptible strains at enrollment and during the recurrent UTI, two women had resistant strains at both enrollment and recurrent UTI and one woman had a resistant strain at enrollment but a susceptible strain during the recurrent UTI.<br><br>The microbiological cure rate at the first follow-up visit (five days after treatment) was 96% in the ciprofloxacin treatment group compared to 81% of patients who received cefpodoxime (difference, 15%; 95% CI, 8 to 23).<br><br>Among women infected with strains that were susceptible to the study antibiotic, the microbiological cure rates were 97% for women receiving ciprofloxacin and 81% for women treated with cefpodoxime (difference, 16%; 95% CI, 9 to 24).<br><br>Vaginal *E. coli* colonization was present at enrollment in 82% of women in both treatment groups. By the first follow-up visit, 16% of the women in the ciprofloxacin group compared to 40% in the cefpodoxime group had vaginal *E. coli* colonization. At the 30-day follow-up visit colonization was reported in 29% |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
|---|---|---|---|---|
| | | | | of the ciprofloxacin group compared to 40% of the cefpodoxime group. The development of subsequent UTI did not correlate with the presence of vaginal *E coli* colonization at the first follow-up visit. |
| **Miscellaneous** | | | | |
| Falagas et al[71]<br><br>Linezolid<br><br>vs<br><br>glycopeptides (vancomycin and teicoplanin*) or β-lactams (amoxicillin/clavulanate, ampicillin/sulbactam, cefadroxil, ceftriaxone, oxacillin, dicloxacillin) | MA<br><br>Patients with complicated skin and soft tissue infections, Gram-positive infections, uncomplicated skin and soft tissue infections, nosocomial pneumonia, community-acquired pneumonia or MRSA infections | N=6,093<br><br>Up to 28 days | Primary:<br>Treatment success, all-cause mortality and adverse effects<br><br>Secondary:<br>Treatment duration, microbiological assessment and eradication of Gram-positive cocci | Primary:<br>For all infections, linezolid had significantly higher treatment success with the ITT patients (OR, 1.23; 95% CI, 1.06 to 1.42; *P* value not reported) and clinically assessed patients (OR, 1.41; 95% CI, 1.11 to 1.81; *P*=0.006) compared to the glycopeptides or β-lactams. When only the blinded RCTs were analyzed, there was no significant difference between the treatments in the ITT patients (OR, 1.14; 95% CI, 0.95 to 1.38; *P* value not reported) and in clinically assessed patients (OR, 1.15; 95% CI, 0.89 to 1.48; *P*=0.29). Additionally, there was no significant difference in treatment success in the clinically assessed patients when linezolid was compared to vancomycin alone (OR, 1.44; 95% CI, 0.90 to 2.30) or β-lactams (OR, 11.34; 95% CI, 0.99 to 1.81).<br><br>For the skin and soft tissue infections in the clinically assessed patients, linezolid had significantly higher treatment success compared to glycopeptides or β-lactams (OR, 1.67; 95% CI, 1.31 to 2.12; *P*<0.0001).<br><br>For bacteremia in the clinically assessed patients, linezolid had significantly higher treatment success compared to glycopeptides or β-lactams (OR, 2.07; 95% CI, 1.13 to 3.78; *P*=0.02).<br><br>There was no significant difference between linezolid and glycopeptides or β-lactams for the treatment of pneumonia in the clinically assessed patients (OR, 1.03; 95% CI, 0.75 to 1.42; *P*=0.84). This was similar for the subset of patients with nosocomial pneumonia (OR, 1.05; 95% CI, 0.75 to 1.46; *P* value not reported).<br><br>There was no significant difference in mortality between linezolid and glycopeptides or β-lactams in the ITT patients (OR, 0.97; 95% CI, 0.79 to 1.19; *P* value not reported).<br><br>There were more adverse events with linezolid compared to glycopeptides or β-lactams in the ITT patients; although, the difference was not significant (OR, |

| Study and Drug Regimen | Study Design and Demographics | Sample Size and Study Duration | End Points | Results |
|---|---|---|---|---|
| | | | | 1.40; 95% CI, 0.95 to 2.06; *P*=0.09). Linezolid was associated with significantly more thrombocytopenia in the ITT patients compared to glycopeptides or β-lactams (OR, 11.75; 95% CI, 3.66 to 37.57; *P*<0.0001).<br><br>Secondary:<br>For all Gram-positive infections in the microbiologically assessed patients, linezolid had significantly higher treatment success compared to glycopeptides or β-lactams (OR, 1.34; 95% CI, 1.05 to 1.72; *P*=0.02).<br><br>Linezolid was associated with higher rates eradication rates for *S aureus* in the microbiologically assessed patients compared to the other antibiotics (OR, 1.81; 95% CI, 1.40 to 2.34; *P*<0.00001).<br><br>There was no significant differences in eradication rate for MRSA between linezolid and the other antibiotics (OR, 1.69; 95% CI, 0.84 to 3.41; *P*=0.014). There was also no significant difference between linezolid and vancomycin in patients with MRSA pneumonia (OR, 1.26; 95% CI, 0.54 to 2.96; *P* value not reported).<br><br>There was no significant difference in eradication of enterococci species between linezolid and the other antibiotics (OR, 0.95; 95% CI, 0.33 to 2.73; *P*=0.93). |

Drug regimen abbreviations: BID=twice daily, QD=daily, QID=four times daily, TID=three times daily
Study abbreviations: AC=active controlled, CI=confidence interval, DB=double blind, DD=double-dummy, DR=dose-response, ITT=intent-to-treat, MA=meta analysis, MC=multi-center, NS=non-significant, OL=open label, OR=odds ratio, PC=placebo-controlled, PG=parallel group, PRO=prospective, SB=single blinded, RCT=randomized controlled trial
Miscellaneous abbreviations: COPD=chronic obstructive pulmonary disease, MRSA=methicillin-resistant *Staphylococcus aureus*

## Special Populations

**Table 6. Special Populations**[1-7]

| Generic Name | Population and Precaution | | | | |
|---|---|---|---|---|---|
| | Elderly/ Children | Renal Dysfunction | Hepatic Dysfunction | Pregnancy Category | Excreted in Breast Milk |
| Cefdinir | No dosage adjustment required in the elderly.<br><br>Safety and efficacy have not been established in children <6 months of age. | A dose of 300 mg once daily is recommended in patients with creatinine clearance <30 mL/minute.<br><br>The recommended initial dose in patients on chronic hemodialysis is 300 mg or 7 mg/kg every other day. | Not studied in hepatic disease; no dosage adjustment is expected to be required. | B | Not detected in milk after single 600 mg dose. |
| Cefditoren | No dosage adjustment required in the elderly.<br><br>Safety and efficacy have not been established in children <12 years of age. | A dose of 200 mg twice a day is recommended in patients with creatinine clearance 30 to 49 mL/minute and 200 mg once daily in patients with creatinine clearance <30 mL/minute. | No dosage adjustment required in patients with mild to moderate hepatic impairment. Not studied in severe hepatic impairment. | B | Unknown; use with caution. |
| Cefixime | No dosage adjustment required in the elderly.<br><br>Safety and efficacy in children <6 months of age have not been established. | Reduce recommended dose by 35% in patients with creatinine clearance 21 to 59 mL/minute or on hemodialysis; use oral suspension.<br><br>Reduce recommended dose by 50% in patients with creatinine clearance <20 mL/minute or those on continuous peritoneal dialysis. | No dosage adjustment required. | B | Unknown; use with caution. |
| Cefpodoxime | No dosage adjustment required in the elderly. | The dosing interval should be extended to every 24 hours in patients with creatinine clearance | No dosage adjustment required. | B | Yes |

| Generic Name | Population and Precaution | | | | |
|---|---|---|---|---|---|
| | Elderly/ Children | Renal Dysfunction | Hepatic Dysfunction | Pregnancy Category | Excreted in Breast Milk |
| | Safety and efficacy in children <2 months of age have not been established. | <30 mL/minute.<br><br>In patients maintained on hemodialysis, the dose frequency should be three times/week after hemodialysis. | | | |
| Ceftibuten | No dosage adjustment required in the elderly.<br><br>Safety and efficacy in children <6 months of age have not been established. | A dose of 200 mg every 24 hours or 4.5 mg/kg is recommended in patients with creatinine clearance 30 to 49 mL/minute.<br><br>A dose of 100 mg every 24 hours or 2.25 mg/kg is recommended in patients with creatinine clearance 5 to 29 mL/minute.<br><br>Patients undergoing hemodialysis should be given 400 mg or 9 mg/kg at the end of each session. | No dosage adjustment required. | B | Unknown; use with caution. |

## Adverse Drug Events

**Table 7. Adverse Drug Events (%)**[1-7]

| Adverse Event | Cefdinir | Cefditoren | Cefixime | Cefpodoxime | Ceftibuten |
|---|---|---|---|---|---|
| **Cardiovascular** | | | | | |
| Cardiac failure | ✔ | - | - | - | - |
| Chest pain | ✔ | - | - | <1 | - |
| Congestive heart failure | - | - | - | <1 | - |
| Hypertension | ✔ | - | - | <1 | - |
| Hypotension | - | - | - | <1 | - |
| Myocardial infarction | ✔ | - | - | - | - |
| Palpitation | - | - | - | <1 | - |
| Vasodilation | - | - | - | <1 | - |
| **Central Nervous System** | | | | | |
| Abnormal dreams | - | >0.1<1.0 | - | <1 | - |
| Agitation | - | - | - | - | >0.1<1.0 |
| Anxiety | - | - | - | <1 | - |
| Asthenia | 0.2 | >0.1<1.0 | - | <1 | - |
| Cerebral infarction | - | - | - | <1 | - |

| Adverse Event | Cefdinir | Cefditoren | Cefixime | Cefpodoxime | Ceftibuten |
|---|---|---|---|---|---|
| Confusion | ✔ | - | - | <1 | - |
| Dizziness | 0.3 | >0.1<1.0 | <2 | <1 | 1 |
| Fatigue | - | - | - | <1 | >0.1<1.0 |
| Fever | ✔ | >0.1<1.0 | - | <1 | >0.1<1.0 |
| Hallucinations | - | - | - | <1 | - |
| Headache | 2 | 2 to 3 | <2 | 1 | 3 |
| Hyperactivity | 0.2 | ✔ | - | <1 | >0.1<1.0 |
| Hypertonia | - | ✔ | - | - | - |
| Impaired concentration | - | - | - | <1 | - |
| Insomnia | 0.2 | >0.1<1.0 | - | <1 | >0.1<1.0 |
| Involuntary movements | ✔ | - | - | - | - |
| Irritable behavior | - | - | - | - | >0.1<1.0 |
| Migraine | - | - | - | <1 | - |
| Nervousness | - | >0.1<1.0 | - | <1 | - |
| Nightmares | - | - | - | <1 | - |
| Paresthesias | - | - | - | <1 | >0.1<1.0 |
| Psychosis | - | - | - | - | ✔ |
| Rigors | - | - | - | - | >0.1<1.0 |
| Seizures | ✔ | ✔ | <2 | ✔ | ✔ |
| Shakiness | - | - | - | <1 | - |
| Somnolence | 0.2 | >0.1<1.0 | - | <1 | >0.1<1.0 |
| Syncope | - | - | - | <1 | - |
| Vertigo | - | - | - | <1 | - |
| **Dermatological** | | | | | |
| Acne | - | - | - | <1 | - |
| Desquamation | - | - | - | <1 | - |
| Diaper rash | - | - | - | 2 | >0.1<1.0 |
| Dry skin | - | - | - | <1 | - |
| Erythema multiforme | ✔ | ✔ | <2 | ✔ | - |
| Erythema nodosum | ✔ | - | - | - | - |
| Exfoliative dermatitis | ✔ | - | - | <1 | - |
| Fungal dermatitis | - | - | - | <1 | - |
| Hair loss | - | - | - | <1 | - |
| Pruritus | 0.2 | >0.1<1.0 | <2 | <1 | >0.1<1.0 |
| Rash | 0.2 to 8.0 | >0.1<1.0 | <2 | 1.8 | >0.1<1.0 |
| Stevens-Johnson syndrome | ✔ | ✔ | <2 | ✔ | ✔ |
| Sunburn | - | - | - | <1 | - |
| Toxic epidermal necrolysis | ✔ | ✔ | <2 | ✔ | ✔ |
| Urticaria | - | >0.1<1.0 | <2 | <1 | >0.1<1.0 |
| **Gastrointestinal** | | | | | |
| Abdominal cramps | - | - | - | <1 | - |
| Abdominal pain | 0.8 to 1.0 | 2 | 3 | 1.2 | 1 to 2 |
| Abnormal stools | 0.2 to 0.3 | - | - | - | - |
| Aphasia | - | - | - | - | ✔ |
| Appetite increased | - | >0.1<1.0 | - | - | - |
| Bloody diarrhea | ✔ | - | - | - | - |
| Colitis | - | ✔ | <2 | - | - |
| Colitis, hemorrhagic | ✔ | - | - | - | - |
| Constipation | 0.3 | >0.1<1.0 | - | <1 | >0.1<1.0 |
| Cutaneous moniliasis | 0.9 | - | - | - | - |

| Adverse Event | Cefdinir | Cefditoren | Cefixime | Cefpodoxime | Ceftibuten |
|---|---|---|---|---|---|
| Diarrhea | 4 to 17 | 11 to 15 | 16 | 1.2 to 12.8 | 3 to 4 |
| Dry throat | - | - | - | <1 | - |
| Dyspepsia | 0.2 to 0.7 | 1 to 2 | 3 | <1 | 2 |
| Enterocolitis, acute | ✔ | - | - | - | - |
| Eructation | - | >0.1<1.0 | - | <1 | >0.1<1.0 |
| Flatulence | 0.7 | >0.1<1.0 | 4 | <1 | >0.1<1.0 |
| Gastritis | - | - | - | <1 | - |
| Gastrointestinal disorder | - | >0.1<1.0 | - | <1 | - |
| Ileus | ✔ | - | - | - | - |
| Loose stools | - | - | 6 | - | >0.1to 2.0 |
| Melena | - | - | - | - | ✔ |
| Nausea/vomiting | 0.2 to 3.0 | 1 to 6 | 7 | 1.4 to 3.3 | 2 to 4 |
| Oral lesions | - | - | - | <1 | - |
| Oral moniliasis | - | >0.1<1.0 | - | <1 | - |
| Peptic ulcer | ✔ | - | - | - | - |
| Pseudomembranous colitis | ✔ | >0.1<1.0 | ✔ | <1 | ✔ |
| Rectal disorders | - | - | - | <1 | - |
| Rectorrhagia with hypotension | - | - | - | ✔ | - |
| Stomatitis | ✔ | >0.1<1.0 | - | <1 | - |
| Taste perversion | - | >0.1<1.0 | - | <1 | >0.1<1.0 |
| Tenesmus | - | - | - | <1 | - |
| Tongue disorder | - | - | - | <1 | - |
| Tooth ache | - | - | - | <1 | - |
| Tooth disorders | - | - | - | <1 | - |
| Ulcerative colitis | - | - | - | ✔ | - |
| Upper gastrointestinal bleed | ✔ | - | - | - | - |
| **Genitourinary** | | | | | |
| Dysmenorrhea | - | - | - | - | - |
| Dysuria | - | - | - | <1 | >0.1<1.0 |
| Genital moniliasis | 0.2 to 4.0 | 3 to 6 | <2 | 1 | - |
| Genital pruritus | - | ✔ | <2 | - | - |
| Hematuria | - | 3.0 to 3.1 | - | <1 | >0.1<1.0 |
| Leukorrhea | 0.2 | >0.1<1.0 | - | - | - |
| Metrorrhagia | - | - | - | <1 | - |
| Nocturia | - | - | - | <1 | - |
| Penile infection | - | - | - | <1 | - |
| Urine white blood cells increased | - | 2.3 | - | - | - |
| Urinary frequency | - | - | - | <1 | - |
| Urinary tract infection | - | - | - | <1 | - |
| Vaginal pain | - | - | - | <1 | - |
| Vaginitis | 1 | >0.1<1.0 | <2 | <1 | - |
| Vulvovaginal infections | - | - | - | 1.3 | - |
| **Hematological** | | | | | |
| Agranulocytosis | ✔ | ✔ | - | ✔ | ✔ |
| Albumin decreased | - | >0.1<1.0 | - | <1 | - |
| Anemia | - | - | - | <1 | - |
| Aplastic anemia | ✔ | ✔ | <2 | ✔ | ✔ |
| Basophilia | - | - | - | <1 | - |
| Bleeding tendency | ✔ | - | - | - | - |
| Coagulation disorder | ✔ | >0.1<1.0 | - | - | - |

| Adverse Event | Cefdinir | Cefditoren | Cefixime | Cefpodoxime | Ceftibuten |
|---|---|---|---|---|---|
| Disseminated intravascular coagulation | ✔ | - | - | ✔ | - |
| Eosinophilia | 0.7 to 1.0 | >0.1<1.0 | <2 | <1 | 3 |
| Granulocytopenia | ✔ | - | - | - | - |
| Granulocytosis | - | - | - | <1 | - |
| Hematocrit decreased | 0.2 | 2.1 to 2.2 | - | <1 | - |
| Hemoglobin decreased | 0.3 to 0.5 | >0.1<1.0 | - | <1 | 1 to 2 |
| Hemolytic anemia | ✔ | ✔ | <2 | ✔ | ✔ |
| Hemorrhage | ✔ | ✔ | <2 | ✔ | ✔ |
| Idiopathic thrombocytopenia purpura | ✔ | - | - | <1 | - |
| Leukocytosis | - | - | - | <1 | - |
| Leukopenia | 0.3 | >0.1<1.0 | <2 | <1 | >0.1<1.0 |
| Lymphocytes decreased | 0.8 to 1.0 | - | - | <1 | - |
| Lymphocytes increased | 0.2 to 2.0 | >0.1<1.0 | - | - | - |
| Monocytes increased | 0.4 | - | - | <1 | - |
| Neutropenia | ✔ | >0.1<1.0 | <2 | <1 | ✔ |
| Pancytopenia | ✔ | ✔ | - | ✔ | ✔ |
| Platelets increased | 0.2 to 1.0 | >0.1<1.0 | - | - | >0.1≤1.0 |
| Polymorphonuclear neutrophils decreased | 0.2 to 1.0 | - | - | - | - |
| Polymorphonuclear neutrophils increased | 0.3 to 1.0 | - | - | - | - |
| Positive Coomb's test | - | ✔ | - | <1 | - |
| Prothrombin time increased | - | ✔ | <2 | <1 | - |
| Thrombocythemia | - | >0.1<1.0 | - | <1 | - |
| Thrombocytopenia | ✔ | - | <2 | <1 | >0.1<1.0 |
| Thrombocytosis | - | - | - | <1 | - |
| White blood cells decreased | 0.7 | >0.1<1.0 | - | - | - |
| White blood cells increased | 0.3 to 0.9 | >0.1<1.0 | - | - | - |
| **Hepatic** | | | | | |
| Acute liver injury | - | - | - | ✔ | - |
| Abnormal liver enzymes | 0.2 to 1.0 | >0.1<1.0 | <2 | <1 | >0.1<1.0 |
| Bilirubin increased | - | ✔ | <2 | <1 | 1 |
| Cholestasis | ✔ | ✔ | <2 | ✔ | ✔ |
| Hepatic dysfunction | ✔ | ✔ | <2 | ✔ | - |
| Hepatitis, transient | ✔ | - | <2 | - | - |
| Jaundice | ✔ | - | <2 | - | ✔ |
| **Musculoskeletal** | | | | | |
| Back pain | - | - | - | <1 | - |
| Myalgia | - | >0.1<1.0 | - | <1 | - |
| Rhabdomyolysis | ✔ | - | - | - | - |
| **Renal** | | | | | |
| Acute renal failure | ✔ | - | <2 | - | - |
| Blood urea nitrogen increased | 0.3 | >0.1<1.0 | <2 | <1 | 2 to 4 |
| Creatinine increased | - | ✔ | <2 | <1 | >0.1<1.0 |
| Microhematuria | 1 | - | - | - | - |
| Nephropathy | ✔ | - | - | - | - |
| Purpuric nephritis | - | - | - | ✔ | - |
| Renal insufficiency | ✔ | ✔ | <2 | ✔ | ✔ |
| Toxic nephropathy | ✔ | ✔ | <2 | ✔ | ✔ |

| Adverse Event | Cefdinir | Cefditoren | Cefixime | Cefpodoxime | Ceftibuten |
|---|---|---|---|---|---|
| Urine glucose increased | 0.9 | - | - | - | - |
| Urine leukocytes increased | 0.5 to 2.0 | - | - | - | - |
| Urine protein increased | 1 to 2 | >0.1<1.0 | - | <1 | - |
| Urine pH increased | 0.2 to 0.8 | - | - | - | - |
| Urine specific gravity increased or decreased | 0.1 to 0.6 | - | - | - | - |
| **Respiratory** | | | | | |
| Acute respiratory failure | ✔ | - | - | - | - |
| Asthma | - | >0.1<1.0 | - | <1 | - |
| Asthmatic shock | ✔ | - | - | - | - |
| Bronchitis | - | - | - | <1 | - |
| Cough | - | - | - | <1 | - |
| Dyspnea | - | - | - | <1 | >0.1<1.0 |
| Epistaxis | - | - | - | <1 | - |
| Nasal congestion | - | - | - | - | >0.1<1.0 |
| Pharyngitis | - | >0.1<1.0 | - | - | - |
| Pleural effusion | - | - | - | <1 | - |
| Pneumonia | - | - | - | <1 | - |
| Pneumonia, drug induced | ✔ | - | - | - | - |
| Pneumonia, eosinophilic | ✔ | - | - | - | - |
| Pneumonia, idiopathic interstitial | ✔ | - | - | - | - |
| Pulmonary infiltrate | - | - | - | ✔ | - |
| Rhinitis | - | >0.1<1.0 | - | <1 | - |
| Sinusitis | - | >0.1<1.0 | - | <1 | - |
| Stridor | - | - | - | - | ✔ |
| Wheezing | - | - | - | <1 | - |
| **Miscellaneous** | | | | | |
| Abnormal microbiological tests | - | - | - | <1 | - |
| Abscess | - | - | - | <1 | - |
| Allergic vasculitis | ✔ | - | - | - | - |
| Anaphylaxis | ✔ | ✔ | <2 | ✔ | ✔ |
| Angioedema | ✔ | ✔ | <2 | - | - |
| Anorexia | 0.3 | >0.1<1.0 | - | <1 | >0.1<1.0 |
| Bacterial infections | - | - | - | <1 | - |
| Bicarbonate decreased | 0.6 to 1.0 | - | - | - | - |
| Calcium decreased | - | >0.1<1.0 | - | - | - |
| Chills | - | - | - | <1 | - |
| Chloride decreased | - | >0.1<1.0 | - | - | - |
| Conjunctivitis | ✔ | - | - | - | - |
| Dehydration | - | - | - | <1 | >0.1<1.0 |
| Dry mouth | 0.3 | >0.1<1.0 | - | <1 | >0.1<1.0 |
| Edema | ✔ | - | - | <1 | - |
| Eye irritation | - | - | - | <1 | - |
| Eyelid dermatitis | - | - | - | ✔ | - |
| Feeling of suffocation | ✔ | - | - | - | - |
| Fungal infection | - | >0.1<1.0 | - | <1 | - |
| Glucose increased | 0.9 | - | - | - | - |
| Gout | - | - | - | <1 | - |
| Hematoma | - | - | - | <1 | - |
| Hyperglycemia | - | 1.1 to 1.8 | - | <1 | - |
| Hyperlipidemia | - | >0.1<1.0 | - | - | - |

| Adverse Event | Cefdinir | Cefditoren | Cefixime | Cefpodoxime | Ceftibuten |
|---|---|---|---|---|---|
| Hyperkalemia | 0.2 to 0.3 | >0.1<1.0 | - | <1 | - |
| Hypoglycemia | - | - | - | <1 | - |
| Hypoproteinemia | - | - | - | <1 | - |
| In-utero exposure with miscarriage | - | - | - | ✔ | - |
| Loss of consciousness | ✔ | - | - | - | - |
| Malaise | - | - | - | <1 | - |
| Moniliasis | - | - | - | - | >0.1<1.0 |
| Pain | - | >0.1<1.0 | - | <1 | - |
| Parasitic infections | - | - | - | <1 | - |
| Peripheral edema | - | >0.1<1.0 | - | <1 | - |
| Phosphorus decreased | 0.3 to 0.4 | >0.1<1.0 | - | - | - |
| Phosphorus increased | 0.6 to 0.9 | - | - | - | - |
| Serum sickness-like reaction | ✔ | ✔ | <2 | ✔ | ✔ |
| Shock | ✔ | - | - | - | - |
| Sodium decreased | - | >0.1<1.0 | - | <1 | - |
| Superinfection | ✔ | ✔ | <2 | - | - |
| Sweating | - | >0.1<1.0 | - | <1 | - |
| Thirst | - | >0.1<1.0 | - | <1 | - |
| Tinnitus | - | - | - | <1 | - |
| Weight increased | - | - | - | <1 | - |

✔ Percent not specified.
- Event not reported.

## Contraindications

**Table 8. Contraindications**[1-7]

| Contraindications | Cefdinir | Cefditoren | Cefixime | Cefpodoxime | Ceftibuten |
|---|---|---|---|---|---|
| Allergy to cephalosporins | ✔ | ✔ | ✔ | ✔ | ✔ |
| Carnitine deficiency or inborn errors of metabolism | - | ✔ | - | - | - |
| Milk protein hypersensitivity; do not administer (not lactose intolerance) | - | - | - | - | - |

## Warnings/Precautions

**Table 9. Warnings and Precautions**[1-7]

| Warnings and Precautions | Cefdinir | Cefditoren | Cefixime | Cefpodoxime | Ceftibuten |
|---|---|---|---|---|---|
| Hypersensitivity reactions; determine whether the patient has had previous hypersensitivity reactions to cephalosporins, penicillins, or other drugs | ✔ | ✔ | ✔ | ✔ | ✔ |
| Pseudomembranous colitis been reported with nearly all antibacterial agents | ✔ | ✔ | ✔ | ✔ | ✔ |
| Renal function impairment; lower doses should be used in this patient population | ✔ | - | ✔ | ✔ | ✔ |
| Superinfection; prolonged | ✔ | ✔ | ✔ | ✔ | ✔ |

| Warnings and Precautions | Cefdinir | Cefditoren | Cefixime | Cefpodoxime | Ceftibuten |
|---|---|---|---|---|---|
| treatment with broad-spectrum antibiotics may result in the emergence and overgrowth of resistant organisms | | | | | |
| Resistance; antibiotic use in the absence of a bacterial infection or for prophylaxis is unlikely to provide benefit to the patient and increases the risk of developing drug-resistant bacteria | ✔ | ✔ | ✔ | - | - |
| Not recommended when prolonged antibiotic treatment is necessary, as other pivalate-containing compounds have caused carnitine deficiency when used over several months | - | ✔ | - | - | - |
| Coagulation abnormalities; cephalosporins may be associated with a fall in prothrombin activity | - | ✔ | ✔ | - | - |
| Seizures; cephalosporins have been implicated in triggering seizures, particularly in patients with renal impairment when the dosage was not reduced | ✔ | ✔ | ✔ | ✔ | ✔ |
| Special risk patients; use with caution in individuals with histories of gastrointestinal disease, particularly colitis | ✔ | - | ✔ | - | ✔ |

## Drug Interactions

**Table 10. Drug interactions**[1-7]

| Generic Name | Interacting Medication or Disease | Potential Result |
|---|---|---|
| Cephalosporins (cefdinir, cefditoren, cefpodoxime) | Antacids (Aluminum- or magnesium-containing) | Plasma concentrations and antimicrobial effects of cephalosporins may be decreased by antacids. |
| Cephalosporins (cefditoren, cefpodoxime, ceftibuten) | H-2 antagonists | Plasma concentrations affected; clinical significance is unknown. |
| Cefdinir | Iron | Absorption of cefdinir is impaired when coadministered with iron salts. |

## Dosage and Administration

**Table 11. Dosing and Administration**[1-7]

| Generic Name | Usual Adult Dose | Usual Pediatric Dose | Availability |
|---|---|---|---|
| Cefdinir | Acute exacerbations of chronic bronchitis (bacterial):<br>300 mg every 12 hours (5 to 10 days) or 600 mg QD (10 days)<br><br>Acute maxillary sinusitis:<br>300 mg every 12 hours (10 days) or 600 mg QD (10 days)<br><br>Community-acquired pneumonia:<br>300 mg every 12 hours (10 days)<br><br>Pharyngitis and/or tonsillitis:<br>300 mg every 12 hours (5 to 10 days) or 600 mg QD (10 days)<br><br>Uncomplicated skin and skin structure infections:<br>300 mg every 12 hours (10 days) | Acute otitis media (six months to 12 years of age):<br>7 mg/kg every 12 hours (5 to 10 days) or 14 mg/kg QD (10 days)*<br><br>Acute maxillary sinusitis (six months to 12 years of age):<br>7 mg/kg every 12 hours (10 days) or 14 mg/kg QD (10 days)*<br><br>Pharyngitis and/or tonsillitis (six months to 12 years of age):<br>7 mg/kg every 12 hours (5 to 10 days) or 14 mg/kg QD (10 days)*<br><br>Uncomplicated skin and skin structure infections (six months to 12 years of age):<br>7 mg/kg every 12 hours (10 days)*<br><br>Safety and efficacy have not been established in children <6 months of age. | Capsule:<br>300 mg<br><br>Powder for oral suspension:<br>125 mg/5 mL<br>250 mg/5 mL |
| Cefditoren | Acute exacerbations of chronic bronchitis (bacterial):<br>400 mg BID (10 days)<br><br>Community-acquired pneumonia:<br>400 mg BID (14 days)<br><br>Pharyngitis and/or tonsillitis:<br>200 mg BID (10 days)<br><br>Uncomplicated skin and skin structure infections:<br>200 mg BID (10 days) | Safety and efficacy have not been established in children <12 years of age. | Tablet:<br>200 mg<br>400 mg |
| Cefixime | Gonorrhea, uncomplicated (cervical/urethral):<br>400 mg as a single dose or one-half tablet (200 mg) every 12 hours | Urinary tract infections, acute bacterial exacerbations of chronic bronchitis, pharyngitis and/or tonsillitis, acute | Powder for oral suspension:<br>100 mg/5 mL<br>200 mg/5 mL |

| Generic Name | Usual Adult Dose | Usual Pediatric Dose | Availability |
|---|---|---|---|
| | Urinary tract infections, acute bacterial exacerbations of chronic bronchitis, pharyngitis and/or tonsillitis, acute bronchitis and otitis media†:<br>200 mg every 12 hours or 400 mg QD | bronchitis and otitis media (six months to 12 years of age)†:<br>4 mg/kg every 12 hours or 8 mg/kg QD‡ | Tablet:<br>400 mg |
| Cefpodoxime | Acute ano-rectal infections in women:<br>200 mg (single dose)<br><br>Acute bacterial exacerbations of chronic bronchitis; acute Maxillary sinusitis:<br>200 mg every 12 hours (10 days)<br><br>Community-acquired pneumonia:<br>200 mg every 12 hours (14 days)<br><br>Gonorrhea and rectal gonococcal infections (men and women):<br>200 mg (single dose)<br><br>Pharyngitis and/or tonsillitis:<br>100 mg every 12 hours (5 to 10 days)<br><br>Uncomplicated urinary tract infections:<br>100 mg every 12 hours (7 days)<br><br>Uncomplicated skin and skin structure infections:<br>400 mg every 12 hours (7 to 14 days) | Acute maxillary sinusitis (two months to 12 years of age):<br>5 mg/kg every 12 hours; maximum 200 mg/dose and 400 mg/day (5 days)<br><br>Otitis media (two months to 12 years of age):<br>5 mg/kg every 12 hours; maximum 200 mg/dose and 400 mg/day (10 days)<br><br>Pharyngitis and/or tonsillitis(two months to 12 years of age):<br>5 mg/kg every 12 hours; maximum 100 mg/dose and 200 mg/day (5 to 10 days)<br><br>Safety and efficacy in children <2 months of age have not been established. | Powder for oral suspension:<br>50 mg/5 mL<br>100 mg/5 mL<br><br>Tablet:<br>100 mg<br>200 mg |
| Ceftibuten | Acute bacterial exacerbations of chronic bronchitis<br>400 mg QD (10 days)<br><br>Otitis media:<br>400 mg QD (10 days)<br><br>Pharyngitis and/or tonsillitis:<br>400 mg QD (10 days) | Acute bacterial exacerbations of chronic bronchitis, otitis media and pharyngitis and/or tonsillitis§:<br>9 mg/kg QD; maximum 400 mg QD (10 days)<br><br>Safety and efficacy in children <6 months of age have not been established. | Capsule:<br>400 mg<br><br>Powder for oral suspension:<br>90 mg/5 mL<br>180 mg/5 mL |

*Patients weighing ≥43 kg should receive the maximum daily dose of 600 mg.
†Otitis media should be treated with cefixime suspension, not cefixime tablets. The suspension results in higher peak blood levels compared to the tablet when administered at the same dose.
‡Children weighting >50 kg should receive the recommended adult dose of cefixime.
§Patients weighing ≥45 kg should receive the maximum daily dose of 400 mg.
BID=twice daily, QD=once daily

## Clinical Guidelines

The clinical guidelines contained in Table 12 are summarized globally and are not limited to the role of the third generation cephalosporins. However, the summary of the Chronic Obstructive Pulmonary Disease (COPD) guidelines focuses only on the treatment of exacerbations which have a bacterial component. The global treatment strategy for COPD is not discussed in this summary.

**Table 12. Clinical Guidelines**

| Clinical Guideline | Recommendations |
|---|---|
| Infectious Diseases Society of America/ American Thoracic Society: **Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults (2007)**[11] | Empirical antimicrobial therapy<br>• Recommendations are generally for a class of antibiotics rather than for a specific drug, unless outcome data clearly favor one drug.<br>• Because overall efficacy remains good for many classes of agents, the more potent drugs are given preference because of their benefit in decreasing the risk of selection for antibiotic resistance.<br>• Outpatient treatment<br>o Previously healthy and no risk factors for drug-resistant *Streptococcus pneumoniae* infection:<br>▪ Macrolide (azithromycin, clarithromycin, or erythromycin).<br>▪ Doxycycline.<br>o Presence of comorbidities, such as chronic heart, lung, liver, or renal disease; diabetes mellitus; alcoholism; malignancies; asplenia; immunosuppressing conditions or use of immunosuppressing drugs; use of antimicrobials within the previous three months (in which case an alternative from a different class should be selected); or other risks for drug-resistant Streptococcus pneumoniae infection:<br>▪ Respiratory fluoroquinolone (moxifloxacin, gemifloxacin, or levofloxacin).<br>▪ β-lactam plus a macrolide (high-dose amoxicillin or amoxicillin/clavulanate is preferred; alternatives include ceftriaxone, cefpodoxime, and cefuroxime; doxycycline is an alternative to the macrolide).<br>o In regions with a high rate of infection with high-level macrolide-resistant *Streptococcus pneumoniae,* consider the use of alternative agents listed above for any patient, including those without comorbidities.<br>• Inpatient, non-intensive care unit treatment<br>o Respiratory fluoroquinolone.<br>o β-lactam plus a macrolide (preferred β-lactam agents include cefotaxime, ceftriaxone, and ampicillin; ertapenem for selected patients; with doxycycline as an alternative to the macrolide. A respiratory fluoroquinolone should be used for penicillin-allergic patients).<br>• Inpatient, intensive care unit treatment<br>o β-lactam (cefotaxime, ceftriaxone, or ampicillin/sulbactam) plus either azithromycin or a fluoroquinolone (for penicillin-allergic patients, a respiratory fluoroquinolone and aztreonam are recommended).<br>o For *Pseudomonas* infection, use an antipneumococcal, antipseudomonal β-lactam (piperacillin/tazobactam, cefepime, imipenem, or meropenem) plus either ciprofloxacin or levofloxacin; OR<br>o Antipneumococcal, antipseudomonal β-lactam (listed above) plus |

| Clinical Guideline | Recommendations |
|---|---|
| | an aminoglycoside and azithromycin; OR<br>o Antipneumococcal, antipseudomonal β-lactam (listed above) plus an aminoglycoside and an antipneumococcal fluoroquinolone (for penicillin-allergic patients, substitute aztreonam for the above β-lactam).<br>• For community-acquired methicillin-resistant *Staphylococcus aureus* infection, add vancomycin or linezolid. |
| American College of Chest Physicians: **Management of Community-Acquired Pneumonia in the Home: An American College of Chest Physicians Clinical Position Statement (2005)**[12] | • The oral route for medications is recommended if the patient can tolerate it, and if the availability and activity of the agents are adequate.<br>• Severity of illness, patient age, comorbidities, concomitant medications, and ease of administration are all factors that can impact the empiric treatment decision.<br>• The use of a macrolide, doxycycline, or fluoroquinolone antibacterial agent is recommended by both the Infectious Disease Society of America and the American Thoracic Society consensus guidelines as appropriate empiric outpatient treatment for low-risk patients.<br>• Amoxicillin/clavulanate and some second generation cephalosporins (cefuroxime, cefpodoxime, or cefprozil) are alternatives for low-risk patients.<br>• A patient who is at high risk either because of complicated comorbidities or extensive prior antibiotic use may be a candidate for treatment with a β-lactam/macrolide combination or an antipneumococcal fluoroquinolone.<br>• Double therapy with either a β-lactam/macrolide combination or a β-lactam/antipneumococcal fluoroquinolone should be considered in patients who would normally be considered for intensive care unit admission but have chosen to remain in the home. |
| American Family Physicians: **Diagnosis and Management of Community-Acquired Pneumonia in Adults (2011)**[13] | • Because the exact causative organism is not identified in many patients with community-acquired pneumonia, treatment is usually empiric.<br>• Macrolides (e.g., azithromycin, clarithromycin, doxycycline) can be used for outpatients with no cardiopulmonary disease or recent antibiotic use.<br>• Outpatients with comorbidities or antibiotic use in past three months (use an antibiotic from a different class than the one used in the past three months):<br>o A respiratory fluoroquinolone (levofloxacin, gemifloxacin, or moxifloxacin, or a beta-lactam antibiotic (high-dose amoxicillin, amoxicillin/clavulanate, or cefpodoxime) plus a macrolide.<br>• Inpatients, non-intensive-care unit:<br>o A respiratory fluoroquinolone, or a beta-lactam antibiotic plus a macrolide.<br>• Inpatients, intensive care unit:<br>o A beta-lactam antibiotic (ceftriaxone, cefotaxime, or ampicillin/sulbactam), plus azithromycin or a respiratory fluoroquinolone.<br>• Risk factors for *Pseudomonas*:<br>o A beta-lactam antibiotic (piperacillin/tazobactam, cefepime, imipenem/cilastatin, meropenem, or doripenem), plus either ciprofloxacin or levofloxacin OR<br>o The above beta-lactam antibiotic plus an aminoglycoside and azithromycin OR<br>o The above beta-lactam antibiotic plus an aminoglycoside and an antipneumococcal respiratory fluoroquinolone. |

| Clinical Guideline | Recommendations |
|---|---|
| | • Risk factors for methicillin-resistant *Staphylococcus aureus:*<br>o Vancomycin or linezolid.<br>• Influenza virus:<br>o Oseltamivir or zanamivir |
| Infectious Diseases Society of America: **The Management of Community-Acquired Pneumonia in Infants and Children Older Than 3 Months of Age: Clinical Practice Guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America (2011)**[14] | <u>Outpatient treatment</u><br>• Antimicrobial therapy is not routinely required for preschool-aged children with community-acquired pneumonia, because viral pathogens are responsible for the great majority of clinical disease.<br>• Amoxicillin should be used as first-line therapy for previously healthy, appropriately immunized infants and preschool children with mild to moderate community-acquired pneumonia suspected to be of bacterial origin. Amoxicillin provides appropriate coverage for *Streptococcus pneumoniae*.<br>• For patients allergic to amoxicillin, the following agents are considered alternative treatment options:<br>o Second- or third-generation cephalosporin (cefpodoxime, cefuroxime, cefprozil).<br>o Levofloxacin (oral therapy).<br>o Linezolid (oral therapy).<br>• Macrolide antibiotics should be prescribed for treatment of children (primarily school-aged children and adolescents) evaluated in an outpatient setting with findings compatible with community-acquired pneumonia caused by atypical pathogens.<br><br><u>Inpatient treatment</u><br>• Ampicillin or penicillin G should be administered to the fully immunized infant or school-aged child admitted to a hospital ward with community-acquired pneumonia when local epidemiologic data document lack of substantial high-level penicillin resistance for invasive *Streptococcus pneumoniae*.<br>• Empiric therapy with a third-generation parenteral cephalosporin (ceftriaxone or cefotaxime) should be prescribed for hospitalized infants and children who are not fully immunized, in regions where local epidemiology of invasive pneumococcal strains documents high-level penicillin resistance, or for infants and children with life-threatening infection, including those with empyema.<br>• Non–β-lactam agents, such as vancomycin, have not been shown to be more effective than third-generation cephalosporins in the treatment of pneumococcal pneumonia for the degree of resistance noted currently in North America.<br>• Empiric combination therapy with a macrolide (oral or parenteral), in addition to a β-lactam antibiotic, should be prescribed for the hospitalized child for whom *Mycoplasma pneumoniae* and *Chlamydophila pneumoniae* are significant considerations.<br>• Vancomycin or clindamycin (based on local susceptibility data) should be provided in addition to β-lactam therapy if clinical, laboratory, or imaging characteristics are consistent with infection caused by *Staphylococcus aureus*. |
| American Academy of **Diagnosis and Management of Acute Otitis Media (2013)**[15] | <u>Observation option</u><br>• Observation without use of antibacterial agents in a child with unilateral acute otitis media is an option for selected children based on age, illness severity, and assurance of follow-up after joint decision-making with the |

| Clinical Guideline | Recommendations |
|---|---|
| | parent(s)/caregiver. The "observation option" for acute otitis media refers to deferring antibacterial treatment of selected children for 48 to 72 hours and limiting management to symptomatic relief. This option should be limited to otherwise healthy children six months and older without severe symptoms at presentation.<br><br>Antibacterial options - temperature <39°C without severe otalgia<br>• For the initial treatment of otitis media, the recommended agent is amoxicillin 80 to 90 mg/kg/day.<br>• For treatment failures at 48 to 72 hours after initial management with observation option, the recommended agent is amoxicillin 80 to 90 mg/kg/day.<br>• For treatment failures at 48 to 72 hours after initial management with antibacterial agents, the recommended agent is amoxicillin/clavulanate.<br><br>Antibacterial options - temperature ≥39°C and/or severe otalgia<br>• For the initial treatment of otitis media, the recommended agent is amoxicillin/clavulanate.<br>• For treatment failures at 48 to 72 hours after initial management with observation option, the recommended agent is amoxicillin/clavulanate.<br>• For treatment failures at 48 to 72 hours after initial management with antibacterial agents, the recommended agent is ceftriaxone for three days. |
| Infectious Diseases Society of America: **Clinical Practice Guideline for the Diagnosis and Management of Group A Streptococcal Pharyngitis: 2012 Update by the Infectious Diseases Society of America (2012)**[16] | • Patients with acute streptococcal pharyngitis should receive therapy with an antimicrobial agent in a dose and for a duration that is likely to eradicate the infecting organism from the pharynx.<br>• Penicillin or amoxicillin are the agents of choice because of their proven efficacy, safety, and narrow spectrum.<br>• Treatment of acute streptococcal pharyngitis is penicillin-allergic patients should include a first generation cephalosporin for ten days, clindamycin or clarithromycin for ten days or azithromycin for five days.<br>• Intramuscular administration of benzathine penicillin G is preferred for patients who are unlikely to complete a full 10- day course of oral therapy.<br>• Most oral antibiotic therapy must be administered for the conventional 10 days to achieve maximal rates of pharyngeal eradication of group A streptococci.<br>• When multiple episodes occur over the course of months or years, it may be difficult to differentiate viral pharyngitis in a *Streptococcus* carrier from true group A streptococcal pharyngitis. Therapy with certain antimicrobial agents, such as clindamycin and amoxicillin/clavulanate, may be beneficial, because they have been shown to yield high rates of eradication of streptococci from the pharynx under these particular circumstances. |
| American Heart Association: **Prevention of Rheumatic Fever and Diagnosis and Treatment of Acute Streptococcal Pharyngitis (2009)**[17] | Primary prevention (treatment of Streptococcal tonsillopharyngitis)<br>• The oral antibiotics of choice are penicillin V and amoxicillin.<br>• Penicillin V, amoxicillin or benzathine penicillin G is recommended.<br>• In patients allergic to penicillin, a narrow spectrum cephalosporin, clindamycin, azithromycin or clarithromycin may be used.<br>• In symptomatic patients who fail an initial course of penicillin, retreatment with a narrow spectrum cephalosporin, clindamycin, |

| Clinical Guideline | Recommendations |
|---|---|
| | amoxicillin/clavulanate or a combination of penicillin plus rifampin is recommended.<br>• In clinical trials, a once-daily amoxicillin (Moxatag®) was shown to be effective for group A streptococcal pharyngitis. It has the advantage of being dosed once-daily which may enhance adherence.<br><br>Secondary prevention (prevention of recurrent attacks of rheumatic fever)<br>• Benzathine penicillin G, penicillin V or sulfadiazine are recommended.<br>In patients allergic to penicillin, a macrolide or azalide are recommended. |
| American Academy of Pediatrics: **Clinical Practice Guideline for the Diagnosis and Management of Acute Bacterial Sinusitis in Children Aged 1 to 18 Years (2013)**[18] | • Antibiotic therapy should be prescribed for acute bacterial sinusitis in children with severe onset or worsening course (signs, symptoms or both).<br>• Antibiotic therapy or additional outpatient observation for three days should be utilized for children with persistent illness (nasal discharge of any quality, cough or both for at least 10 days).<br>• When a decision has been made to initiate antibiotic therapy for the treatment of acute bacterial sinusitis, amoxicillin with or without clavulanate is considered first-line.<br>• For children ≥2 years of age with uncomplicated acute bacterial sinusitis that is mild to moderate in severity that do not attend child care and have not received antibiotics in the previous four weeks, amoxicillin 45 mg/kg/day in two divided doses is recommended. In communities with high prevalence of Streptococcus pneumoniae (>10%, including intermediate and high level resistance), amoxicillin may be initiated at 80 to 90 mg/kg/day in two divided doses with a maximum of 2 g per dose.<br>• Patients with moderate to severe illness and those <2 years of age who are attending child care or have recently received antibiotics, amoxicillin/clavulanate (80 to 90 mg/kg/day of amoxicillin with 6.4 mg/kg/day of clavulanate to a maximum of 2 g per dose) may be used.<br>• A single dose of ceftriaxone 50 mg/kg intravenous or intramuscular may be used for children who are vomiting, unable to tolerate oral medication or unlikely to adhere to initial doses of antibiotic. |

| Clinical Guideline | Recommendations |
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| Infectious Disease Society of America: **Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the Infectious Diseases Society of America (2014)**[20] | Impetigo and ecthyma<br>• Gram stain and culture of the pus or exudates from skin lesions of impetigo and ecthyma are recommended to help identify whether *Staphylococcus aureus* and/or a β-hemolytic *Streptococcus* is the cause, but treatment without these studies is reasonable in typical cases.<br>• Bullous and nonbullous impetigo can be treated with oral or topical antimicrobials, but oral therapy is recommended for patients with numerous lesions or in outbreaks affecting several people to help decrease transmission of infection. Treatment for ecthyma should be an oral antimicrobial.<br>o Treatment of bullous and nonbullous impetigo should be with either mupirocin or retapamulin twice daily for five days.<br>o Oral therapy for ecthyma or impetigo should be a seven-day regimen with an agent active against *Staphylococcus aureus* unless cultures yield streptococci alone (when oral penicillin is the recommended agent.<br>o Because *Staphylococcus aureus* isolates from impetigo and ecthyma are usually methicillin susceptible, dicloxacillin or cephalexin is recommended. When methicillin-resistant *Staphylococcus aureus* (MRSA) is suspected or confirmed, doxycycline, clindamycin, or sulfamethoxazole/trimethoprim is recommended.<br>o Systemic antimicrobials should be used for infections during outbreaks of poststreptococcal glomerulonephritis to help eliminate nephritogenic strains of *Streptococcus pyogenes* from the community.<br><br>Treatment for purulent skin and soft tissue infections (SSTIs) (cutaneous abscesses, furuncles, carbuncles, and inflamed epidermoid cysts)<br>• Gram stain and culture of pus from carbuncles and abscesses are recommended, but treatment without these studies is reasonable in typical cases.<br>• Gram stain and culture of pus from inflamed epidermoid cysts are not recommended.<br>• Incision and drainage is the recommended treatment for inflamed epidermoid cysts, carbuncles, abscesses, and large furuncles.<br>• The decision to administer antibiotics directed against *Staphylococcus aureus* as an adjunct to incision and drainage should be made based upon presence or absence of systemic inflammatory response syndrome (SIRS), such as temperature >38°C or <36°C, tachypnea >24 breaths per minute, tachycardia >90 beats per minute, or white blood cell count >12 000 or <400 cells/μL. An antibiotic active against MRSA is recommended for patients with carbuncles or abscesses who have failed initial antibiotic treatment or have markedly impaired host defenses or in patients with SIRS and hypotension.<br><br>Recurrent skin abscesses<br>• A recurrent abscess at a site of previous infection should prompt a search for local causes such as a pilonidal cyst, hidradenitis suppurativa, or foreign material.<br>• Recurrent abscesses should be drained and cultured early in the course of infection. |

| Clinical Guideline | Recommendations |
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| | • After obtaining cultures of recurrent abscess, treat with a 5- to 10-day course of an antibiotic active against the pathogen isolated.<br>• Consider a five-day decolonization regimen twice daily of intranasal mupirocin, daily chlorhexidine washes, and daily decontamination of personal items such as towels, sheets, and clothes for recurrent *Staphylococcus aureus* infection.<br>• Adult patients should be evaluated for neutrophil disorders if recurrent abscesses began in early childhood.<br><br>Erysipelas and cellulitis<br>• Cultures of blood or cutaneous aspirates, biopsies, or swabs are not routinely recommended.<br>• Cultures of blood are recommended, and cultures and microscopic examination of cutaneous aspirates, biopsies, or swabs should be considered in patients with malignancy on chemotherapy, neutropenia, severe cell-mediated immunodeficiency, immersion injuries, and animal bites.<br>• Typical cases of cellulitis without systemic signs of infection should receive an antimicrobial agent that is active against streptococci. For cellulitis with systemic signs of infection, systemic antibiotics are indicated. Many clinicians could include coverage against methicillin-susceptible *Staphylococcus aureus* (MSSA). For patients whose cellulitis is associated with penetrating trauma, evidence of MRSA infection elsewhere, nasal colonization with MRSA, injection drug use, or SIRS, vancomycin or another antimicrobial effective against both MRSA and streptococci is recommended. In severely compromised patients, broad-spectrum antimicrobial coverage may be considered. Vancomycin plus either piperacillin/tazobactam or imipenem/meropenem is recommended as a reasonable empiric regimen for severe infections.<br>• The recommended duration of antimicrobial therapy is five days, but treatment should be extended if the infection has not improved within this time period.<br>• Elevation of the affected area and treatment of predisposing factors, such as edema or underlying cutaneous disorders, are recommended.<br>• In lower-extremity cellulitis, clinicians should carefully examine the interdigital toe spaces because treating fissuring, scaling, or maceration may eradicate colonization with pathogens and reduce the incidence of recurrent infection.<br>• Outpatient therapy is recommended for patients who do not have SIRS, altered mental status, or hemodynamic. Hospitalization is recommended if there is concern for a deeper or necrotizing infection, for patients with poor adherence to therapy, for infection in a severely immunocompromised patient, or if outpatient treatment is failing.<br>• Systemic corticosteroids (e.g., prednisone 40 mg daily for seven days) could be considered in nondiabetic adult patients with cellulitis.<br><br>Recurrent cellulitis<br>• Identify and treat predisposing conditions such as edema, obesity, eczema, venous insufficiency, and toe web abnormalities. These practices should be performed as part of routine patient care and during the acute stage of cellulitis.<br>• Administration of prophylactic antibiotics, such as oral penicillin or |

| Clinical Guideline | Recommendations |
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| | erythromycin twice daily for 4 to 52 weeks, or intramuscular benzathine penicillin every two to four weeks, should be considered in patients who have three to four episodes of cellulitis per year despite attempts to treat or control predisposing factors. This should be continued so long as the predisposing factors persist.<br><br>Surgical site infections<br>• Suture removal plus incision and drainage should be performed for surgical site infections.<br>• Adjunctive systemic antimicrobial therapy is not routinely indicated, but in conjunction with incision and drainage may be beneficial for surgical site infections associated with a significant systemic response, such as erythema and induration extending >5 cm from the wound edge, temperature >38.5°C, heart rate >110 beats/minute, or white blood cell (WBC) count >12 000/µL.<br>• A brief course of systemic antimicrobial therapy is indicated in patients with surgical site infections following clean operations on the trunk, head and neck, or extremities that also have systemic signs of infection.<br>• A first-generation cephalosporin or an antistaphylococcal penicillin for MSSA, or vancomycin, linezolid, daptomycin, telavancin, or ceftaroline where risk factors for MRSA are high (nasal colonization, prior MRSA infection, recent hospitalization, recent antibiotics), is recommended.<br>• Agents active against gram-negative bacteria and anaerobes, such as a cephalosporin or fluoroquinolone in combination with metronidazole, are recommended for infections following operations on the axilla, gastrointestinal tract, perineum, or female genital tract.<br><br>Necrotizing fasciitis, including Fournier gangrene<br>• Prompt surgical consultation is recommended for patients with aggressive infections associated with signs of systemic toxicity or suspicion of necrotizing fasciitis or gas gangrene (severe nonpurulent).<br>• Empiric antibiotic treatment should be broad (e.g., vancomycin or linezolid plus piperacillin/tazobactam or a carbapenem; or plus ceftriaxone and metronidazole), as the etiology can be polymicrobial (mixed aerobic–anaerobic microbes) or monomicrobial (group A streptococci, community-acquired MRSA).<br>• Penicillin plus clindamycin is recommended for treatment of documented group A streptococcal necrotizing fasciitis.<br><br>Dog or cat bites<br>• Preemptive early antimicrobial therapy for three to five days is recommended for patients who (a) are immunocompromised; (b) are asplenic; (c) have advanced liver disease; (d) have preexisting or resultant edema of the affected area; (e) have moderate to severe injuries, especially to the hand or face; or (f) have injuries that may have penetrated the periosteum or joint capsule.<br>• Postexposure prophylaxis for rabies may be indicated; consultation with local health officials is recommended to determine if vaccination should be initiated.<br><br>Animal bite–related wounds<br>• An antimicrobial agent or agents active against both aerobic and |

| Clinical Guideline | Recommendations |
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| | anaerobic bacteria such as amoxicillin/clavulanate should be used.<br>• Tetanus toxoid should be administered to patients without toxoid vaccination within 10 years. Tetanus, diphtheria, and tetanus (Tdap) is preferred over Tetanus and diphtheria (Td) if the former has not been previously given.<br><br>Erysipeloid<br>• Penicillin or amoxicillin for 7 to 10 days is recommended for treatment of erysipeloid.<br><br>Immunocompromised patients<br>• In addition to infection, differential diagnosis of skin lesions should include drug eruption, cutaneous infiltration with the underlying malignancy, chemotherapy- or radiation-induced reactions, Sweet syndrome, erythema multiforme, leukocytoclastic vasculitis, and graft-versus-host disease among allogeneic transplant recipients.<br>• Differential diagnosis for infection of skin lesions should include bacterial, fungal, viral, and parasitic agents.<br>• Biopsy or aspiration of the lesion to obtain material for histological and microbiological evaluation should always be implemented as an early diagnostic step. |
| Infectious Diseases Society of America: **Diagnosis and Treatment of Diabetic Foot Infections (2012)**[21] | • Clinically uninfected wounds should not be treated with antibiotic therapy.<br>• Antibiotic therapy is recommended for all infected wounds but this is often insufficient unless combined with appropriate wound care.<br>• Clinicians should select an empiric antibiotic regimen based on the severity of the infection and the likely etiologic agent.<br>o For mild to moderate infections in patients who have not recently received antibiotic treatment, therapy should target aerobic gram-positive cocci.<br>o For most severe infections, broad-spectrum empiric antibiotic therapy should be started, pending culture results and antibiotic susceptibility data.<br>o Empiric therapy directed at *Pseudomonas aeruginosa* is usually unnecessary except for patients with risk factors for true infection with this organism.<br>o Consider providing empiric therapy directed against *methicillin-resistant Staphylococcus aureus* (MRSA) in a patient with a prior history of MRSA infection or colonization or when the local prevalence of MRSA colonization or infection is high or if the infection is clinically severe.<br>• Targeted therapy should be based on the results of culture and sensitivity testing of a wound specimen as well as the patient's clinical response to the empiric regimen.<br>• The route of therapy should be based on infection severity. Parenteral therapy is recommended for all severe, and some moderate, diabetic foot infections, at least initially, switching to oral agents when the patient is systemically well and culture results are available. Clinicians can use oral antibiotics with high bioavailability alone in most mild, and in many moderate, infections and topical therapy for selected mild superficial infections.<br>• Antibiotic therapy should continue until, but not after the resolution |

| Clinical Guideline | Recommendations |
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| | infection, but not through complete healing of the wound. An initial antibiotic course for a soft tissue infection of about one to two weeks for mild infections and two to three weeks for moderate to severe infections.<br>• Based on the results of the available studies, no single drug or combination of agents appears to be superior to any others.<br>• For infections of mild severity, the recommended antibiotic agents include: dicloxacillin, clindamycin, cephalexin, levofloxacin and amoxicillin-clavulanate. Doxycycline or trimethoprim/sulfamethoxazole may be used for MRSA.<br>• For moderate or severe infections, the recommended antibiotic agents include: levofloxacin, cefoxitin, ceftriaxone, ampicillin-sulbactam, moxifloxacin, ertapenem, tigecycline, levofloxacin or ciprofloxacin with clindamycin, Imipenem-cilastatin. If MRSA is suspected, linezolid, daptomycin or vancomycin may be used. Piperacillin-tazobactam may be an option if *Pseudomonas aeruginosa* is a concern. |
| American College of Obstetricians and Gynecologists: **Practice Bulletin: Treatment of Urinary Tract Infections in Nonpregnant Women (2008)**[22] | • Most urinary tract infections are caused by *E coli* (80 to 90%).<br>• Other causes of urinary tract infections include *Staphylococcus saprophyticus*, *Proteus*, *Pseudomonas*, *Klebsiella* and *Enterobacter* species.<br>• Treatment options include sulfamethoxazole/trimethoprim (preferred), trimethoprim, ciprofloxacin, levofloxacin, norfloxacin, gatifloxacin (all three-day regimens), nitrofurantoin macrocrystals, nitrofurantoin monohydrate/macrocrystals (seven-day regimens) and fosfomycin tromethamine (single dose).<br>• First generation cephalosporins and amoxicillin are less effective than the above agents due to resistance and rapid excretion from the urinary tract.<br>• B-lactams are not first-line therapy in acute cystitis unless the causative organism is gram-positive, in which case amoxicillin or amoxicillin/clavulanate may be used.<br>• Women with frequent recurrences may be treated with once daily nitrofurantoin, norfloxacin, ciprofloxacin, trimethoprim, sulfamethoxazole/trimethoprim or any other agent listed above for six to 12 months and then be reassessed.<br>• Sulfamethoxazole/trimethoprim is considered the preferred treatment for uncomplicated cystitis except in areas where resistance is common.<br>• Fluoroquinolones should not be used first-line in areas where sulfamethoxazole/trimethoprim resistance is uncommon.<br>• Acute pyelonephritis in acutely ill patients should be treated with parenteral broad-spectrum antibiotics. If gram-positive organisms are suspected, amoxicillin, ampicillin or a cephalosporin may be used. In other cases β-lactams are no longer recommended.<br>• First-line treatment for pyelonephritis is now a fluoroquinolone. sulfamethoxazole/trimethoprim may be used in areas of low resistance.<br>• Parenteral treatment options include an aminoglycoside with ampicillin or piperacillin, a first generation cephalosporin, aztreonam, piperacillin/tazobactam, or a parenteral fluoroquinolone alone or in combination. |
| Infectious Diseases | Acute uncomplicated bacterial cystitis |

| Clinical Guideline | Recommendations |
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| Society of America: **International Clinical Practice Guidelines for the Treatment of Uncomplicated Acute Bacterial Cystitis and Acute Pyelonephritis in Women: A 2010 Update by the Infectious Disease Society of America and the European Society for Microbiology and Infectious Disease (2011)**[23] | • Taking into consideration availability, allergy history and tolerance the following antimicrobials are recommended: nitrofurantoin monohydrate/macrocrystals, sulfamethoxazole/trimethoprim, fosfomycin, pivmecillinam*.<br>• Fluoroquinolones (ofloxacin, ciprofloxacin and levofloxacin) are recommended as alternative agents if the above agents cannot be used. Although highly efficacious, fluoroquinolones (ofloxacin, ciprofloxacin and levofloxacin) should be reserved for important uses other than acute cystitis due to increasing resistance.<br>• β-lactams (amoxicillin/clavulanate, cefdinir, and cefpodoxime) are also recommended as alternative agents. Due to poor efficacy and antimicrobial resistance, amoxicillin and ampicillin should not be used as monotherapy.<br><br><u>Acute pyelonephritis</u><br>• In patients not requiring hospitalization and where the prevalence of resistance in the community is not known to exceed 10%, oral ciprofloxacin with or without an initial intravenous loading dose is appropriate.<br>• An initial one-time intravenous dose of a long-acting parenteral antimicrobial, such as ceftriaxone or consolidated 24-hour dose of an aminoglycoside is recommended if prevalence of fluoroquinolone resistance exceeds 10%.<br>• In patients not requiring hospitalization and where the prevalence of resistance in the community is not known to exceed 10%, a once-daily fluoroquinolone (e.g., ciprofloxacin, levofloxacin) is appropriate.<br>• If the pathogen is known to be susceptible, oral sulfamethoxazole/trimethoprim is recommended. When the susceptibility is not known, an initial intravenous dose of a long-acting parenteral antimicrobial, such as ceftriaxone or consolidated 24-hour dose of an aminoglycoside is recommended.<br>• Oral β-lactam agents are less effective than other available agents. Therefore if an oral β-lactam agent is used, an initial intravenous dose of a long-acting parenteral antimicrobial, such as ceftriaxone or consolidated 24-hour dose of an aminoglycoside is recommended.<br>• For women with pyelonephritis requiring hospitalization, an intravenous antimicrobial regimen, such as a fluoroquinolone; an aminoglycoside, with or without ampicillin; an extended-spectrum cephalosporin or extended-spectrum penicillin, with or without an aminoglycoside; or a carbapenem should be initial treatment. |
| Centers for Disease Control and Prevention: **Sexually Transmitted Diseases Treatment Guidelines (2010)**[24] | <u>Chancroid</u><br>• Azithromcyin, ceftriaxone, ciprofloxacin (contraindicated in pregnant or lactating women) or erythromycin are recommended treatment strategies.<br><br><u>Genital herpes simplex virus</u><br>• First episodes should be treated with acyclovir, famciclovir, or valcyclovir.<br>• Acyclovir, famciclovir or valcyclovir may be used as suppressive therapy, though famciclovir may be somewhat less effective for suppression of viral shedding. Ease of administration and cost are important considerations for prolonged treatment. |

| Clinical Guideline | Recommendations |
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| | • Episodic treatment requires initiation of therapy within one day of lesion onset or during the prodrome that precedes outbreak.<br>• Intravenous acyclovir is recommended for severe disease.<br><br>Granuloma inguinale<br>• Doxycycline is recommended.<br>• Alternative agents include azithromycin, ciprofloxacin, erythromycin or sulfamethoxazole/trimethoprim.<br>• The addition of an aminoglycoside may be considered if improvement is not evident within the first few days of therapy.<br><br>Lymphogranuloma venereum<br>• Doxycycline is recommended.<br>• An alternative agent is erythromycin.<br>• Clinical data are lacking, though azithromycin is probably effective.<br>• Fluoroquinolone treatment may also be effective, though extended treatment intervals are likely required.<br>• Pregnant and lactating women should be treated with erythromycin. Azithromycin may be an alternative but clinical data are lacking.<br><br>Syphilis<br>• Penicillin G is the preferred drug for all stages of syphilis. Alternative agents include doxycycline and tetracycline. Limited studies suggest that ceftriaxone is effective.<br>• Azithromycin may be effective in early syphilis but should only be used when treatment with penicillin G or doxycycline is not feasible. It should not be used in pregnant women and men who have sex with men.<br>• Penicillin G is the only therapy recommended during pregnancy. Pregnant women with an allergy to penicillin should be desensitized.<br>• Benzathine penicillin G is recommended for primary and secondary syphilis.<br>• Infants ≥1 month of age with primary or secondary syphilis should be treated with benzathine penicillin G.<br>• Early latent syphilis should be treated with benzathine penicillin G in patients with normal cerebrospinal fluid examinations.<br>• Late latent syphilis or latent syphilis of unknown duration should be treated with benzathine penicillin G in patients with normal cerebrospinal fluid examinations. Alternative agents include doxycycline or tetracycline.<br>• Patients with tertiary syphilis with no evidence of neurosyphilis should be treated with benzathine penicillin G.<br>• Patients with neurosyphilis should be treated with aqueous crystalline penicillin G. An alternative regimen in patients in whom compliance can be assured is procaine penicillin plus probenecid.<br>• Congenital syphilis:<br>o Proven or highly probably disease with abnormal physical exam, serum quantitative serologic titer fourfold higher than the mother's titer or positive darkfield test of body fluids should be treated with aqueous crystalline penicillin G or procaine penicillin G.<br>o Normal physical exam and serum quantitative tier same or less than fourfold the maternal tier and the mother was not treated, |

| Clinical Guideline | Recommendations |
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| | inadequately treated or has no documentation of treatment or the mother was treated with erythromycin or other non-penicillin regimen or the mother received <4 weeks of treatment before delivery should be treated with aqueous crystalline penicillin G, procaine penicillin G, or benzathine penicillin G.<br>o Normal physical exam with serum quantitative titer the same or less than fourfold the maternal titer and the mother was treated during pregnancy, treatment was appropriate and administered for >4 weeks before delivery and the mother has no evidence of reinfection or relapse should be treated with benzathine penicillin G.<br>• Infants ≥1 month of age identified as having reactive serologic tests for syphilis should be treated with aqueous crystalline penicillin G.<br>• If the child has no clinical manifestations of the disease and the cerebrospinal fluid examination is normal, penicillin G at up to three weekly doses can be considered.<br>• Any child suspected of having congenital syphilis with neurologic involvement should be treated with aqueous crystalline penicillin G.<br>• Infants and children requiring treatment for syphilis who have a history of penicillin allergy or develop an allergic reaction should be desensitized.<br><br>Urethritis<br>• Azithromycin or doxycycline is recommended. Alternative regimens include erythromycin, levofloxacin or ofloxacin.<br>• In the case of recurrent or persistent urethritis, if the patient was compliant with the initial regimen and re-exposure can be excluded, metronidazole or tinidazole plus azithromycin is recommended.<br><br>Cervicitis<br>• Azithromycin or doxycycline is recommended.<br><br>Chlamydia<br>• Azithromycin or doxycycline is recommended.<br>• Alternative agents include erythromycin, levofloxacin or ofloxacin.<br>• Azithromycin or amoxicillin is recommended in pregnant patients. An alternative agent is erythromycin.<br>• Infants with ophthalmia neonatorum should be treated with oral erythromycin.<br>• Infants with pneumonia caused by *Chlamydia trachomatis* should be treated with oral erythromycin.<br>• Children with chlamydial infection should be treated with oral erythromycin (patients weighing <45 kg), azithromycin (patients weighing ≥45 kg and <8 years), or azithromycin or doxycycline (patients ≥8 years of age).<br><br>Gonococcal infections<br>• Patients infected with *Neisseria gonorrhoeae* are frequently coinfected with *C trachomatis* and should be treated for both infections.<br>• Ceftriaxone is recommended. If ceftriaxone is not an option, other regimens include cefixime or single dose injectable cephalosporin regimens plus azithromycin or doxycycline.<br>• Gonococcal infections of the pharynx should be treated with ceftriaxone |

| Clinical Guideline | Recommendations |
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| | plus azithromycin or doxycycline.<br>• Gonococcal conjunctivitis should be treated with ceftriaxone.<br>• Disseminated gonococcal infection should be treated with ceftriaxone. Alternative agents include cefotaxime or ceftizoxime.<br>• Gonococcal meningitis and endocarditis should be treated with ceftriaxone.<br>• Ophthalmia neonatorum should be treated with ceftriaxone.<br>• Gonococcal scalp abscesses should be treated with ceftriaxone or cefotaxime.<br>• Infants born to mothers with untreated gonorrhea should be treated with ceftriaxone.<br>• Children weighing >45 kg should be treated with a regimen recommended for adults.<br>• Children weighing ≤45 kg should be treated with ceftriaxone at an appropriate dose.<br>• Ceftriaxone is recommended in children with bacteremia or arthritis.<br>• Erythromycin ophthalmic ointment is recommended as prophylaxis against ophthalmia neonatorum at birth. If erythromycin is not available, infants at risk can be administered ceftriaxone.<br><br>Bacterial vaginosis<br>• Metronidazole orally or topically or topical clindamycin are recommended.<br>• Alternative agents include oral tinidazole or oral or intravaginal clindamycin.<br>• Intravaginal metronidazole is an option in patients who are unable to tolerate oral metronidazole.<br>• Treatment of all pregnant women with symptoms is recommended. Oral metronidazole or clindamycin is recommended.<br><br>Trichomoniasis<br>• Oral metronidazole or tinidazole is recommended.<br><br>Vulvovaginal candidiasis<br>• Over-the-counter butoconazole, clotrimazole, miconazole or tioconazole are recommended.<br>• Prescription agents include butoconazole, nystatin, terconazole or oral fluconazole.<br>• Oral fluconazole weekly for six months is the recommended treatment for recurrent infection.<br>• Severe vulvovaginal candidiasis should be treated with seven to 14 days of topical therapy or fluconazole in two consecutive doses (second dose 72 hours after initial dose).<br>• Only topical therapies are recommended in pregnancy.<br><br>Pelvic inflammatory disease<br>• Mild to moderate pelvic inflammatory disease should be treated with parenteral or oral therapies.<br>• Recommended parenteral regimen A: cefotetan or cefoxitin plus doxycycline (oral or intravenous).<br>• Recommended parenteral regimen B: clindamycin plus gentamicin. |

| Clinical Guideline | Recommendations |
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| | • Alternative parenteral regimens are ampicillin/sulbactam plus doxycycline (oral or intravenous).<br>• Outpatient oral therapy may be considered in patients with mild to moderate disease. Recommended regimens include ceftriaxone plus doxycycline with or without metronidazole, cefoxitin and probenecid plus doxycycline with or without metronidazole, or another parenteral third generation cephalosporin plus doxycycline with or without metronidazole.<br>• If parenteral cephalosporin therapy is not feasible, fluoroquinolones with or without metronidazole may be considered if the community prevalence and individual risk for gonorrhea are low.<br><br>Epididymitis<br>• Ceftriaxone plus doxycycline is recommended. For acute infections most likely caused by enteric organisms, levofloxacin or ofloxacin are recommended.<br><br>Human papillomavirus<br>• External genital warts:<br>o Podofilox 0.5% solution or gel, imiquimod 5% cream or sinecatechins 15% ointment are recommended as patient-applied treatments.<br>o Cryotherapy with liquid nitrogen or cryoprobe, podophyllin resin, trichloroacetic acid or bichloroacetic acid or surgical removal are recommended as provider-administered treatments.<br>o Alternative regimens include intralesional interferon, photodynamic therapy and topical cidofovir.<br>• Cervical warts:<br>o Biopsy evaluation is recommended to exclude high-grade squamous intraepithelial lesions.<br>• Vaginal warts:<br>o Cryotherapy with liquid nitrogen or trichloroacetic acid or bichloroacetic acid are recommended.<br>• Urethral meatus warts:<br>o Cryotherapy with liquid nitrogen or podophyllin in compound tincture of benzoin is recommended.<br>• Anal warts:<br>o Cryotherapy with liquid nitrogen, trichloroacetic acid or bichloroacetic acid or surgical removal is recommended.<br><br>Proctitis<br>• Ceftriaxone plus doxycycline is recommended.<br><br>Pediculosis pubis<br>• Permethrin or pyrethrins are recommended.<br>• Alternative agents include malathion or ivermectin.<br><br>Scabies<br>• Permethrin or ivermectin are recommended.<br>• Lindane is an alternative agent, not recommended as first-line.<br><br>Prophylaxis after sexual assault |

| Clinical Guideline | Recommendations |
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| | • Hepatitis B vaccination.<br>• Empirical regimen for Chlamydia, gonorrhea and trichomonas.<br>• Emergency contraception.<br>• Ceftriaxone or cefixime plus metronidazole plus azithromycin or doxycycline is the recommended regimen. |
| Global Initiative for Chronic Obstructive Lung Disease: **Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease (2014)**[25] | Management of exacerbations of Chronic Obstructive Pulmonary Disease (COPD) with a bacterial component<br>• Prophylactic, continuous use of antibiotics has been shown to have no effect on the frequency of exacerbations in chronic obstructive pulmonary disease.<br>• There is no current evidence that the use of antibiotics, other than for treating infectious exacerbations of chronic obstructive pulmonary disease and other bacterial infections, is helpful.<br>• Based on current available evidence, antibiotics should be given to:<br>o Patients with exacerbations of chronic obstructive pulmonary disease with the following three cardinal symptoms: dyspnea, sputum volume, and sputum purulence.<br>o Patients with exacerbations of chronic obstructive pulmonary disease with two of the cardinal symptoms, if the increased purulence of sputum is one of the two symptoms.<br>o Patients with a severe exacerbation of chronic obstructive pulmonary disease that requires mechanical ventilation (invasive or noninvasive).<br>• The choice of antibiotic should be based on local bacterial resistance patterns.<br>o Initial empiric treatment may include an aminopenicillin with or without clavulanic acid, macrolide or tetracycline. In patients with frequent exacerbations, severe airflow limitation and/or exacerbations requiring mechanical ventilation, sputum cultures or cultures from other materials from the lung should be performed, as gram-negative bacteria or resistant pathogens that may not be sensitive to the afore-mentioned antibiotics may be present. |
| National Surgical Infection Prevention Project: **Antimicrobial Prophylaxis for Surgery: An Advisory Statement from the National Surgical Infection Prevention Project (2004)**[26] | Sponsoring organizations include the following: American Academy of Orthopaedic Surgeons; American Association of Critical Care Nurses; American Association of Nurse Anesthetists; American College of Surgeons; American College of Osteopathic Surgeons; American Geriatrics Society; American Society of Anesthesiologists; American Society of Colon and Rectal Surgeons; American Society of Health-System Pharmacists; American Society of PeriAnesthesia Nurses; Ascension Health; Association of PeriOperative Registered Nurses; Association for Professionals in Infection Control and Epidemiology; Infectious Diseases Society of America; Medical Letter; Premier; Society for Healthcare Epidemiology of America; Society of Thoracic Surgeons; and Surgical Infection Society.<br><br>Cardiothoracic and vascular surgery<br>• Intravenous cefazolin or intravenous cefuroxime are recommended.<br>• If the patient has a β-lactam allergy, intravenous vancomycin is appropriate and intravenous clindamycin is an alternative.<br><br>Colorectal surgery<br>• Oral neomycin plus oral erythromycin or oral neomycin plus oral |

| Clinical Guideline | Recommendations |
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| | metronidazole are recommended along with administration of a mechanical bowel preparation.<br>• Intravenous cefotetan or intravenous cefoxitin are recommended for parental prophylaxis. Intravenous cefazolin plus oral metronidazole are recommended as a cost-effective alternative.<br>• For patients with a confirmed allergy or adverse reaction to β-lactams, intravenous clindamycin plus intravenous gentamicin, intravenous aztreonam or intravenous ciprofloxacin; intravenous metronidazole plus intravenous gentamicin or intravenous ciprofloxacin are recommended. A single dose of intravenous levofloxacin can be substituted for intravenous ciprofloxacin.<br><br><u>Gynecologic and obstetric surgery</u><br>• Intravenous cefotetan is preferred for abdominal or vaginal hysterectomy. Intravenous cefazolin and intravenous cefoxitin are reasonable alternatives.<br>• Intravenous metronidazole is an alternative, but may be less effective as monotherapy.<br>• For patients with a β-lactam allergy, intravenous clindamycin plus intravenous gentamicin, intravenous aztreonam or intravenous ciprofloxacin; intravenous metronidazole plus intravenous gentamicin or intravenous ciprofloxacin; or intravenous clindamycin monotherapy are recommended. A single dose of intravenous levofloxacin can be substituted for intravenous ciprofloxacin. |

*Agent not currently available in the United States.

## Conclusions

The third generation cephalosporins are used to treat a variety of infections caused by susceptible organisms including skin and skin structure infections, genitourinary tract infections and respiratory tract infections. Third generation cephalosporins are active against streptococci, *Haemophilus influenza* and *Moraxella catarrhalis* and are more active against gram-negative bacilli compared to other cephalosporins.[9,10] They are not as active against susceptible strains of staphylococci as compared to first generation cephalosporins. Treatment guidelines identify third generation cephalosporins as alternative empiric agents for the treatment of community-acquired pneumonia, and as treatment options for infections due to *Enterobacteriaceae*.[11-14] They are considered alternative agents for the treatment of otitis media in patients with non-type 1 penicillin allergies and second-line agents for the treatment of sinusitis and pharyngitis due to penicillin and sulfamethoxazole/trimethoprim resistant bacteria or in patients with non-type 1 penicillin allergies.[15-18] Cefixime is considered a second-line agent for the treatment of gonorrhea after ceftriaxone.[23] The Global Initiative for Chronic Obstructive Lung Disease recommends the use a second or third generation cephalosporin as an alternative to penicillin, ampicillin, amoxicillin, tetracycline or sulfamethoxazole/trimethoprim in patients with chronic obstructive pulmonary disease and mild exacerbations with no risk of a poor outcome.[24]

Clinical trials evaluating the third generation cephalosporins for the treatment of acute exacerbations of chronic bronchitis have not consistently demonstrate significant differences in clinical response or eradication rate when compared to other cephalosporins.[26-31] Verghese and colleagues compared cefixime and cephalexin in the treatment of hospitalized patients with exacerbations of chronic bronchitis and demonstrated significantly better clinical cure rates in patients treated with cefixime compared to cephalexin, though diarrhea occurred more commonly in the cefixime group.[32] Cefixime and cefpodoxime have been shown to be effective in the treatment of gonorrhea in open-label and dose-response studies, and cefixime has been shown to have comparable efficacy when compared to ceftriaxone.[33-37] Asmar et al. compared cefixime and cefpodoxime in the treatment of acute otitis media. No significant differences were observed between agents in clinical or microbiological cure rates.[38] Casey et al conducted a study

of high dose amoxicillin/clavulanic acid (10 day regmin) compared with a standard cefdinir regimen (5 days) and found that the clinical cure rate was statistically greater in the amoxicillin/clavulanic acid group (P=0.001).[66] Other head-to-head studies of the third generation cephalosporins in the treatment of acute otitis media demonstrated no statistically significant differences in efficacy between the agents.[62-65] Studies evaluating the use of the third generation cephalosporins for the treatment of pharyngitis and/or tonsillitis have failed to consistently demonstrate "superiority" of any third generation cephalosporin over penicillin or amoxicillin.[39-46] In the treatment of lower respiratory tract infections including community-acquired pneumonia, no consistently significant differences were observed when the third generation cephalosporins were compared with each other or with cephalosporins in other generations.[47-49] Studies evaluating the treatment of skin and soft tissue infections, sinusitis and urinary tract infections did not consistently demonstrate the "superiority" of any third generation cephalosporin when compared with in-class or with other cephalosporins in other generations.[50-56] Third generation cephalosporins have demonstrated their efficacy in the treatment of bacterial infections of acute bronchitis, chancroid and genital tract infections. [57-59]

Currently cefixime (Suprax®) is the only agent available that does not have a generic option in at least one dosage form or strength.

**References**


1. Cefdinir capsules [package insert]. Dayton (NJ): Aurobindo Pharma USA, Inc.; 2014 Sep.
2. Cefdinir powder for suspension [package insert]. Dayton (NJ): Aurobindo Pharma USA, Inc.; 2014 Mar.
3. Spectracef® tablets [package insert]. Westmount (QC): Vansen Pharma Inc.; 2013 June.
4. Suprax® [package insert]. Baltimore (MD): Lupin Pharma; 2014 Sep.
5. Cefpodoxime tablets [package insert]. Princeton (NJ): Sandoz, Inc.; 2014 Jul.
6. Cefpodoxime granule for suspension [package insert]. Dayton (NJ): Aurobindo Pharma USA, Inc.; 2014 Mar.
7. Cedax® [package insert]. Gonzales (LA): Pernix Therapeutics, LLC; 2010 Apr.
8. Calderwood S. Beta-lactam antibiotics: Mechanisms of action and resistance and adverse effects. In: Hooper DC (Ed). UpToDate [database on the internet]. Waltham (MA): UpToDate; 2014 Apr. [cited 2014 Sep 15]. Available from: http://www.utdol.com/utd/index.do.
9. Calderwod S. Cephalosporins. In: Hooper DC (Ed). UpToDate [database on the internet]. Waltham (MA): UpToDate; 2014 Apr. [cited 2014 Sep 15]. Available from: http://www.utdol.com/utd/idex.do.
10. Antiinfectives 8:00, Antibacterials 8:12, Cephalosporins 8:12.06. In: McEvoy GK ed. American Hospital Formulary Services, AHFS Drug Information 2014 [monograph on the internet]. Bethesda (MD): American Society of Health-System Pharmacists; 2014 [cited 2014 Sep 15]. Available from: http://online.statref.com.
11. Mandell LA, Wunderink RG, Anzueto A, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis. 2007 Mar 1;44 Suppl 2:S27-72.
12. Ramsdell J, Narsavage GL, Fink JB; American College of Chest Physicians' Home Care Network Working Group. Management of community-acquired pneumonia in the home: an American College of Chest Physicians clinical position statement. Chest. 2005 May;127(5):1752-63.
13. Watkins RR, Lemonovich TL. Diagnosis and Management of Community-Acquired Pneumonia in Adults. Am Fam Physician. 2011 Jun 1;83(11):1299-1306.
14. Bradley JS, Byington CL, Shah SS, Alverson B, Carter ER, Harrisn C, et al. The Management of Community-Acquired Pneumonia in Infants and Children Older Than 3 Months of Age: Clinical Practice Guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. Clin Infect Dis. (2011) 53 (7): e25-e76. doi: 10.1093/cid/cir531
15. American Academy of Pediatrics Subcommittee on Management of Acute Otitis Media. Diagnosis and management of acute otitis media. Pediatrics. 2004 May;113(5):1451-65.
16. Shulman ST, Bisno AL, Clegg HW, Gerber MA, Kaplan EL, Lee Grace, et al. Clinical Practice Guideline for the Diagnosis and Management of Group A Streptococcal Pharyngitis: 2012 Update by the Infectious Diseases Society of America. Clin Infect Dis. (2012) doi: 10.1093/cid/cis629
17. Gerber M, Baltimore R, Eaton C, Gewitz M, Rowley A, Shulman S et al. Prevention of rheumatic fever and diagnosis and treatment of acute streptococcus pharyngitis: a scientific statement from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee of the Council on Cardiovascular Disease in the Young, the Interdisciplinary Council on Functional Genomics and Translational Biology, and the Interdisciplinary Council on Quality Care and Outcomes Research: Endorsed by the American Academy of Pediatrics. Circulation. 2009;119:1541-51.
18. Wald ER, Applegate KE, Bordley C, Darrow DH, Glode MP, Marcy M. Clinical Practice Guideline for the Diagnosis and Management of Acute Bacterial Sinusitis in Children Aged 1 to 18 Years. Pediatrics. 2013 Jul;132(1):e262-80.
19. Stevens DL, Bisno AL, Chambers HF, Dellinger EP, Goldstein EJC, Gorbach SL, et al. Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the Infectious Diseases Society of America. Clin Infect Dis. (2014) doi: 10.1093/cid/ciu296
20. Lipsky BA, Berendt AR, Cornia PB, Pile JC, Peters EJ, Armstrong DG, et al. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. Clin Infect Dis. 2012 Jun;54(12):e132-73.
21. American College of Obstetricians and Gynecologists Practice Bulletin: Treatment of urinary tract infections in nonpregnant women. Obstetrics and Gynecology. 2008;111(3):785-94.

22. Gupta K, Hooton TM, Naber KG, Wullt B, Colgan R, Miller LG, et al.; Infectious Diseases Society of America; European Society for Microbiology and Infectious Diseases. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: A 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. Clin Infect Dis. 2011 Mar;52(5):e103-20.
23. Centers for Disease Control and Prevention. Sexually Transmitted Diseases Treatment Guidelines, 2010. MMWR Morb Mortal Wkly Rep. 2010;59(No. RR-12):1-116. Available from: http://www.cdc.gov/std/treatment/2010/. Accessed Jul 31, 2012.
24. Vestbo J, Agusti AG, Anzueto A, Decramer M, Fabbri LM, Jones P, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease (updated 2014). [guideline on the internet]. Global Initiative for Chronic Obstructive Lung Disease, Inc.; 2013 [cited 2014 Sep 15]. Available from: http://www.goldcopd.org/uploads/users/files/GOLD_Report_2014_Jun11.pdf.
25. Bratzler DW, Houck PM; Surgical Infection Prevention Guidelines Writers Workgroup; Antimicrobial prophylaxis for surgery: an advisory statement from the National Surgical Infection Prevention Project. Clin Infect Dis. 2004 Jun 15;38(12):1706-15.
26. Phillips H, Van Hook CJ, Butler T, et al. A comparison of cefpodoxime proxetil and cefaclor in the treatment of acute exacerbation of COPD in adults. Chest. 1993;104(5):1387-91.
27. Chirurgi VA, Edelstein H, Oster SE, et al. Ceftibuten versus cefaclor for the treatment of bronchitis. J Antimicrob Chemother. 1991;28:577-80.
28. Fogarty CM, Bettis RB, Griffin TJ, Keyserling CH, Nemeth MA, Tack KJ. Comparison of a 5 day regimen of cefdinir with a 10 day regimen of cefprozil for treatment of acute exacerbation of chronic bronchitis. J Antimicrob Chemother. 2000;45:851-8.
29. Van Herwaarden C, Langan C, Siemon G, Rudolph C, Keyserling C, Nemeth M, et al. International study comparing cefdinir and cefuroxime axetil in the treatment of patients with acute exacerbation of chronic bronchitis. Int J Infect Dis. 1999;4:26-33.
30. Alvarez-Sala JL, Kardos P, Martínez-Beltrán J, Coronel P, Aguilar L. Clinical and bacteriological efficacy in treatment of acute exacerbations of chronic bronchitis with cefditoren-pivoxil versus cefuroxime-axetil. Antimicrob Agents Chemothera. 2006;50(5):1762-7.
31. Zuck P, Petitpretz P, Geslin P, Rio Y, Leblanc F. Bacteriological eradication of streptococcus pneumoniae from patients with acute exacerbations of chronic bronchitis: cefuroxime axetil versus cefixime. Int J Clin Prac. 1999;53(6):437-43.
32. Verghese A, Roberson D, Kalbfleisch JH, Sarubbi F. Randomized comparative study of cefixime versus cephalexin in acute bacterial exacerbations of chronic bronchitis. Antimicrob Agents Chemother. 1990;34(6):1041-4.
33. Handsfield H, McCormack W, Hook E, Douglas J, Covino J, Verdon M, et al. A comparison of single-dose cefixime with ceftriaxone as a treatment for uncomplicated gonorrhea. NEJM. 1991;325(19):1337-41.
34. Verdon M, Douglas J, Wiggins S, Handfield H. Treatment of uncomplicated gonorrhea with single doses of 200 mg cefixime. Sexually Transmitted Diseases. 1993;20(5):290-3.
35. Plourde P, Tyndall M, Agoki E, Ombette J, Slaney L, D'Costa L, et al. Single-dose cefixime versus single-dose ceftriaxone in the treatment of antimicrobial resistant Neisseria gonorrhoeae infection. Journal of Infectious Diseases. 1992;166(4):919-22.
36. Portilla I, Lutz B, Montalvo M, Mogabag W. Oral cefixime versus intramuscular ceftriaxone in patients with uncomplicated gonococcal infections. Sexually Transmitted Diseases. 1992;19(2):94-8.
37. Novak E, Paxton L, Tubbs H, Turner L, Keck C, Yatsu J. Orally administered cefpodoxime proxetil for treatment of uncomplicated gonococcal urethritis in males: a dose-response study. Antimicrobial agents and Chemotherapy. 1992;1764-5.
38. Asmar BI, Dajani AS, Del Beccaro MA, Mendelman PM. Comparison of cefpodoxime proxetil and cefixime in the treatment of acute otitis media in infants and children. Pediatrics. 1994;94(6):847-52.
39. Nemeth M, McCarty J, Gooch H, Henry D, Keyserling C, Tack K. Comparison of cefdinir and penicillin for the treatment of streptococcal pharyngitis. Clinical Therapeutics. 1999;21(11):1873-81.

40. Tack K, Henry D, Gooch W, Brink D, Keyserling C and the Cefdinir Pharyngitis Study Group. Five-day cefdinir treatment for streptococcal pharyngitis. Antimicrobial Agents and Chemotherapy. 1998;42(5):1073-5.
41. Brook I. A pooled comparison of cefdinir and penicillin in the treatment of group A beta-hemolytic streptococcal pharyngotonsillitis. Clin Therap. 2005;27(8):1266-73.
42. Ozaki T, Nishimura N, Suzuki M, Narita A, Watanabe N, Ahn J, et al. Five-day oral cefditoren pivoxil versus 10-day oral amoxicillin for pediatric group A streptococcal pharyngotonsillitis. J Infect Chemother. 2008;14:213-8.
43. Block S, Hedrick J, Tyler R. Comparative study of the effectiveness of cefixime and penicillin V for the treatment of streptococcal pharyngitis in children and adolescents. Pediatr Infect Dis J. 1992;11:919-25.
44. Adam D, Cefixime Study Group, Hostalek U, Troster K. 5-day cefixime therapy for bacterial pharyngitis and/or tonsillitis: comparison with 10-day penicillin V therapy. Infection. 1995;23(Suppl 2):S83-6.
45. Pichichero ME, Gooch WM, Rodriguez W, Blumer JL, Aronoff SC, Jacobs RF, et al. Effective short-course treatment of acute group A beta-hemolytic streptococcal tonsillopharyngitis. Arch Pediatr Adolesc Med. 1994;148:1053-60.
46. Pichichero M, McLinn S, Gooch M, Rodriguez M, Goldfarb J, Reidenberg B, et al. Ceftibuten vs. penicillin V in group A beta-hemolytic streptococcal pharyngitis. Pediatr Infect Dis J. 1995;14:S102-7.
47. van Zyle L, le Roux J, LaFata J, Volk R, Palo W, Flamm R, et al. Cefditoren pivoxil versus cefpodoxime proxetil for community-acquired pneumonia: results from a multi-center, prospective, randomized, double-blind study. Clin Therap. 2002;24(11):1840-53.
48. Drehobl M, Bianchi P, Keyserling CH, Tack KJ, Griffin TJ. Comparison of cefdinir and cefaclor in the treatment of community-acquired pneumonia. Antimicrob Agents Chemother. 1997;41(7):1579-83.
49. Sengupta J, Mondal AK, Jain P, Garg RD, Mathur NC, Moharana AK. Comparative evaluations of cefpodoxime versus cefixime in children with lower respiratory tract infections. Indian J Pediatr. 2004;71(6):517-21.
50. Tack KJ, Keyserling CH, McCarty J, Hedrick JA. Study of use of cefdinir versus cephalexin for treatment of skin infections in pediatric patients. Antimicrob Agents and Chemother. 1997;41(4):739-42.
51. Tack K, Littlejohn T, Mailloux G, Wolf M, Keyserling C. Cefdinir versus cephalexin for the treatment of skin and skin structure infections. Clin Therap. 1998;20(2):244-56.
52. Stevens DL, Pien F, Drehobol M. Comparison of oral cefpodoxime proxetil and cefaclor in the treatment of skin and soft tissue infections. Diagn Microbiol Infect Dis. 1993;16:123-9.
53. Bucko AD, Hunt BJ, Kidd SL, Hom R. Randomized, double-blind, multicenter comparison of oral cefditoren 200 or 400 mg BID with either cefuroxime 250 mg BID or cefadroxil 500 mg BID for the treatment of uncomplicated skin and skin-structure infections. Clin Ther. 2002;27(7):1134-47.
54. Gehanno P, Depondt J, Barry B, Simonet M, Dewever H. Comparison of cefpodoxime proxetil with cefaclor in the treatment of sinusitis. J Antimicrob Chemother. 1990;26(Suppl E): 87-91.
55. Leigh AP, Nemeth MA, Keyserling CH, Hotary LH, Tack KJ. Cefdinir versus cefaclor in the treatment of uncomplicated urinary tract infection. Clin Ther. 2000;22(7):818-25.
56. Ho MW, Wang FD, Fung CP, Liu CY. Comparative study of ceftibuten and cefixime in the treatment of complicated urinary tract infections. J Microbiol Immunol Infect. 2001;34:185-9.
57. Ziering W, McElvaine P. Randomized comparison of once-daily ceftibuten and twice daily clarithromycin in the treatment of acute exacerbations of chronic bronchitis. Infection 1998;26(1):68-75.
58. Martin DH, Sargent SJ, Wendel GD Jr, McCormack WM, Spier NA, Johnson RB. Comparison of azithromycin and ceftriaxone for the treatment of chancroid. Clin Infect Dis. 1995;21:409-14.
59. French LM, Smaill FM. Antibiotic regimens for endometritis after delivery. Cochrane Database Syst Rev. 2004;18(4):CD001067.
60. Piippo T, Stefansson S, Pitkäjärvi T, Lundberg C. Double-blind comparison of cefixime and cefaclor in the treatment of acute otitis media in children. Scand J Infect Dis. 1991;23:459-65.

61. MacLoughlin GJ, Barreto DG, de la Torre C, Pinetta EA, del Castillo F, Palma L. Cefpodoxime proxetil suspension compared with cefaclor suspension for treatment of acute otitis media in pediatric patients. J Antimicrob Chemother. 1996;37:565-73.
62. Blumer JL, McLinn SE, Deabate A, et al. Multinational multicenter controlled trial comparing ceftibuten with cefaclor for the treatment of acute otitis media. Pediatr Infect Dis J. 1995;14:S115-20.
63. Blumer JL, Mclinn SE, Deabate CA, Kafetzis DA, Perrotta RJ, Salgado O. Five-day cefdinir course vs ten-day cefprozil course for treatment of acute otitis media. Pediatr Infect Dis J. 2000;19(12):S147-S52.
64. Block S, Cifaldi M, Gu Y, Paris M. A comparison of 5 days of therapy with cefdinir or azithromycin in children with acute otitis media: a multicenter, prospective single-blind study. Clin Therap. 2005;27(6):786-94.
65. Mandel E, Rockette H, Paradise J, Bluestone C, Nozza R. Comparative efficacy of erythromycin-sulfisoxazole, cefaclor, amoxicillin or placebo for otitis media with effusion on children. Pediatr Infect Dis J. 1991;10:899-906.
66. Casey JR, Block SL, Hedrick J, Almudevar A, Pichichero M. Comparison of Amoxicillin/Clavulanic Acid High Dose with Cefdinir in the Treatment of Acute Otitis Media. Drugs. 2012 Oct 22;72(15):1991-7. doi: 10.2165/11590320-000000000-00000.
67. Song F, Glenny AM. Antimicrobial prophylaxis in colorectal surgery: a systematic review of randomized controlled trials. Br J Surg. 1998 Sep;85(9):1232-41.
68. Zalmanovici Trestioreanu A, Green H, Paul M, Yaphe J, Leibovici L. Antimicrobial agents for treating uncomplicated urinary tract infection in women. Cochrane Database Syst Rev. 2010 Oct 6;(10):CD007182
69. Bocquet N, Sergent Alaoui A, Jais JP, Gajdos V, Guigonis V, Lacour B, et al. Randomized trial of oral versus sequential IV/oral antibiotic for acute pyelonephritis in children. Pediatrics. 2012 Feb;129(2):e269-75.
70. Hooton TM, Roberts PL, Stapleton AE. Cefpodoxime vs ciprofloxacin for short-course treatment of acute uncomplicated cystitis: a randomized trial. JAMA. 2012 Feb 8;307(6):583-9.
71. Falagas ME, Siempos II, Vardakas KZ. Linezolid versus glycopeptide or beta-lactam for treatment of Gram-positive bacterial infections: meta-analysis of randomized controlled trials. Lancet Infect Dis. 2008 Jan;8(1):53-66.