Therapeutic Class Overview
Second and Third Generation Oral Fluoroquinolones

Therapeutic Class

- **Overview/Summary:** The second and third generation quinolones are approved to treat a variety of infections, including dermatologic, gastrointestinal, genitourinary, respiratory, as well as several miscellaneous infections.[1-10] They are broad-spectrum agents that directly inhibit bacterial deoxyribonucleic acid (DNA) synthesis by blocking the actions of DNA gyrase and topoisomerase IV, which leads to bacterial cell death.[11,12] The quinolones are most active against gram-negative bacilli and gram-negative cocci.[12] Ciprofloxacin has the most potent activity against gram-negative bacteria. Norfloxacin, ciprofloxacin and ofloxacin have limited activity against streptococci and many anaerobes while levofloxacin and moxifloxacin have greater potency against gram-positive cocci, and moxifloxacin has enhanced activity against anaerobic bacteria.[11-12] Gemifloxacin, levofloxacin and moxifloxacin are considered respiratory fluoroquinolones. They possess enhanced activity against *Streptococcus pneumoniae* while maintaining efficacy against *Haemophilus influenzae*, *Moraxella catarrhalis* and atypical pathogens. Resistance to the quinolones is increasing and cross-resistance among the various agents has been documented. Two mechanisms of bacterial resistance have been identified. These include mutations in chromosomal genes (DNA gyrase and/or topoisomerase IV) and altered drug permeability across the bacterial cell membranes.[11-12] Clinical Guidelines support the use of fluoroquinolones in children and adults for a variety of indications including infective endocarditis, valvular heart disease, encephalitis, meningitis, skin and soft tissue infections, infectious diarrhea, as travel medicine, certain sexually transmitted diseases, urinary tract infections, cystitis, pyelonephritis, anthrax, plague, chronic obstructive pulmonary disease, pneumonemia (community and hospital acquired), intra-abdominal infections, cancer-related infections, and prophylaxis.[13-40] This review excludes intravenous dosage forms and encompasses only the oral dosage forms.

Table 1. Medications Included Within the Therapeutic Class Review[4-12]

Generic (Trade Name)	Food and Drug Administration Approved Indications	Dosage Form/Strength	Generic Availability
Second Generation Fluoroquinolones			
Ciprofloxacin (Cipro®*, Cipro XR®*)	Bone and joint infections, urethritis/cervicitis (gonococcal), infectious diarrhea, inhalational anthrax§, intra-abdominal infections, prostatitis, pyelonephritis†, respiratory tract infections (lower), sinusitis, skin and skin-structure infections, typhoid fever, urinary tract infections†,§	Suspension: 250 mg/5 mL 500 mg/5 mL Tablet (extended-release): 500 mg 1,000 mg Tablet (immediate-release): 100 mg 250 mg 500 mg 750 mg	✔
Levofloxacin (Levaquin®*)	Acute exacerbations of chronic bronchitis, inhalational anthrax (post-exposure)#, plague#, pneumonia (community-acquired and nosocomial), prostatitis, pyelonephritis, sinusitis, skin and skin-structure infections, urinary tract infections	Solution: 250 mg/10 mL Tablet: 250 mg 500 mg 750 mg	✔
Norfloxacin	Urethritis/cervicitis (gonococcal),	Tablet:	-

Generic (Trade Name)	Food and Drug Administration Approved Indications	Dosage Form/Strength	Generic Availability
(Noroxin®)	prostatitis, urinary tract infections	400 mg	
Ofloxacin*	Acute exacerbations of chronic bronchitis, cystitis, urethritis/cervicitis (gonococcal and non-gonococcal), pelvic inflammatory disease, pneumonia (community-acquired), prostatitis, skin and skin-structure infections, urinary tract infections	Tablet: 200 mg 300 mg 400 mg	✔
Third Generation Fluoroquinolones			
Gemifloxacin (Factive®)	Acute exacerbations of chronic bronchitis, pneumonia (community-acquired)	Tablet: 320 mg	-
Moxifloxacin (Avelox®*, Avelox ABC Pack®)	Acute exacerbations of chronic bronchitis, Intra-abdominal infections, Pneumonia (community-acquired), sinusitis, skin and skin-structure infections, urethritis/cervicitis (gonococcal), prostatitis, urinary tract infections	Tablet: 400 mg	-

*Generic is available in at least one dosage form or strength.
†Extended-release formulation in addition to instant-release formulation
§Approved for patients ≥1 year of age
#Approved for patients ≥6 months of age

Evidence-based Medicine

- Clinical trials have demonstrated the safety and efficacy of the second and third generation quinolones.[41-71]
- Kaushik et al evaluated azithromycin to ciprofloxacin for the treatment of cholerae in young children aged 2 to 12 years. There was a statistically significant difference in clinical cure favoring azithromycin compared to ciprofloxacin (relative risk [RR], 1.34; 95% confidence interval [CI], 1.16 to 1.54; P<0.001); however, there was not a significant difference in bacteriological success (RR, 1.05; 95% CI, 1.00 to 1.10; P=0.06).[41]
- Clinical trials have demonstrated comparable efficacy and safety profiles among the quinolones for the treatment of skin and soft-tissue infections, genitourinary infections, respiratory tract infections, and other miscellaneous infections.[42-71]

Key Points within the Medication Class

- According to Current Clinical Guidelines:
    - Endocarditis: native/ prostatic valve endocarditis empiric therapy (ciprofloxacin for six months) or treatment of blood culture-negative endocarditis (quinolone for 6 to 18 months).[13-16]
    - Use in prevention of infections after surgery in combination with other antibiotics.[20,39]
    - Recommend use of levofloxacin, moxifloxacin or levofloxacin/ciprofloxacin (in combination with clindamycin) for empiric therapy of diabetic foot infections.[21]
    - First or second line in the treatment of infectious diarrhea, depending on specific cause.[22,24]
    - Quinolones are the first line for chemoprophylaxis and treatment of traveler's diarrhea.[23]
    - Quinolones are first line or alternative therapies for sexually transmitted diseases such as chancroid, chlamydia, epididymitis and non-gonococcal urethritis.[25]
    - Second line for uncomplicated urinary tract infections and first line for acute pyonephritis.[26,27]
    - First line for inhalation anthrax; second line for plauge[28,29]
    - Treatment for acute exacerbation of chronic obstructive pulmonary disease should be based on bacterial resistance patterns, but generally quinolones are not considered first line.[30]

  - Outpatient treatment of community-acquired pneumonia with moxifloxacin, gemifloxacin or levofloxacin is first line in patients with risk factors for drug resistant strains, presence of certain comorbidities, immunosuppressing conditions or use of antimicrobials within the previous three months and as an alternative to patients who cannot tolerate other first line agents.[31-34]
- Other Key Facts:
  - Ofloxacin and levofloxacin are eliminated mostly via the kidney, moxifloxacin is eliminated mostly via the liver, and the others are eliminated via a mix of kidney and liver.[11]
  - Ciprofloxacin (immediate-release) and levofloxacin are the only medications approved for use in patients <18 years of age for certain indications. Ciprofloxacin may be used in patients >1 year of age and levofloxacin is approved for children >6 months of age.[1,4]
  - Moxifloxacin is the only oral quinolone that does not need to adjusted in patients with renal disease.[5]
  - All second and third generation quinolones are available in an oral tablet. Ciprofloxacin is also available in an extended-release tablet. Ciprofloxacin and levofloxacin are formulated as an oral suspension and solution respectively.[1-7]
  - Ciprofloxacin (extended-release), gemifloxacin, levofloxacin and moxifloxacin are approved for once daily dosing.[1-7]
  - Ciprofloxacin, levofloxacin, moxifloxacin and ofloxacin are available in at least one generic formulation.

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Overview/Summary

The second and third generation quinolones are approved to treat a variety of infections, including dermatologic, gastrointestinal, genitourinary, respiratory, as well as several miscellaneous infections.[1-10] They are broad-spectrum agents that directly inhibit bacterial deoxyribonucleic acid (DNA) synthesis by blocking the actions of DNA gyrase and topoisomerase IV, which leads to bacterial cell death.[11,12]

The quinolones are most active against gram-negative bacilli and gram-negative cocci.[12] Ciprofloxacin has the most potent activity against gram-negative bacteria. Norfloxacin, ciprofloxacin and ofloxacin have limited activity against streptococci and many anaerobes while levofloxacin and moxifloxacin have greater potency against gram-positive cocci, and moxifloxacin has enhanced activity against anaerobic bacteria.[11-12] Gemifloxacin, levofloxacin and moxifloxacin are considered respiratory fluoroquinolones. They possess enhanced activity against *Streptococcus pneumoniae* while maintaining efficacy against *Haemophilus influenzae*, *Moraxella catarrhalis* and atypical pathogens. Resistance to the quinolones is increasing and cross-resistance among the various agents has been documented. Two mechanisms of bacterial resistance have been identified. These include mutations in chromosomal genes (DNA gyrase and/or topoisomerase IV) and altered drug permeability across the bacterial cell membranes.[11-12]

Clinical Guidelines support the use of fluoroquinolones in children and adults for a variety of indications including infective endocarditis, valvular heart disease, encephalitis, meningitis, skin and soft tissue infections, infectious diarrhea, as travel medicine, certain sexually transmitted diseases, urinary tract infections, cystitis, pyelonephritis, anthrax, plague, chronic obstructive pulmonary disease, pneumonemia (community and hospital acquired), intra-abdominal infections, cancer-related infections, and prophylaxis.[13-39]

The quinolones that are included in this review are listed in Table 1. This review excludes intravenous dosage forms and encompasses only the oral dosage forms. Ciprofloxacin, levofloxacin, moxifloxacin and ofloxacin are available in at least one generic formulation.

Medications

Table 1. Medications Included Within Class Review

Generic Name (Trade name)	Medication Class	Generic Availability
Ciprofloxacin (Cipro®*, Cipro XR®*)	Second Generation Fluoroquinolone	✔
Gemifloxacin (Factive®)	Third Generation Fluoroquinolone	-
Levofloxacin (Levaquin®*)	Second Generation Fluoroquinolone	✔
Moxifloxacin (Avelox®*, Avelox ABC Pack®)	Third Generation Fluoroquinolone	✔
Norfloxacin (Noroxin®)	Second Generation Fluoroquinolone	-
Ofloxacin*	Second Generation Fluoroquinolone	✔

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

The quinolones have been shown to be active against the strains of microorganisms indicated in Table 2. These agents 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[1-10]

Organism	Ciprofloxacin	Gemifloxacin	Levofloxacin	Moxifloxacin	Norfloxacin	Ofloxacin
Gram-Positive Aerobes						
Bacillus anthracis	✔		✔			
Enterococcus faecalis	✔		✔	✔	✔	
Staphylococcus aureus	✔		✔	✔	✔	✔
Staphylococcus epidermidis	✔		✔		✔	
Staphylococcus saprophyticus	✔		✔		✔	
Streptococcus agalactiae					✔	
Streptococcus anginosus				✔		
Streptococcus constellatus				✔		
Streptococcus pneumoniae	✔	✔	✔	✔		✔
Streptococcus pyogenes	✔		✔	✔		✔
Gram-Negative Aerobes						
Campylobacter jejuni	✔					
Citrobacter divs	✔					✔
Citrobacter freundii	✔				✔	
Enterobacter aerogenes					✔	✔
Enterobacter cloacae	✔		✔	✔	✔	
Escherichia coli	✔		✔	✔	✔	✔
Haemophilus influenzae	✔	✔	✔	✔		✔
Haemophilus parainfluenzae	✔	✔	✔	✔		
Klebsiella pneumoniae	✔	✔	✔	✔	✔	✔
Legionella pneumophila			✔			
Moraxella catarrhalis	✔	✔	✔	✔		
Morganella morganii	✔					
Neisseria gonorrhoeae	✔				✔	✔
Proteus mirabilis	✔		✔	✔	✔	✔
Proteus vulgaris	✔				✔	
Providencia rettgeri	✔					
Providencia stuartii	✔					
Pseudomonas aeruginosa	✔		✔		✔	✔
Salmonella typhi	✔					
Serratia marcescens	✔		✔		✔	
Shigella boydii	✔					
Shigella dysenteriae	✔					
Shigella flexneri	✔					
Shigella sonnei	✔					
Anaerobes						
Bacteroides fragilis				✔		
Bacteroides thetaiotaomicron				✔		
Clostridium perfringens				✔		
Peptostreptococcus species				✔		
Miscellaneous Organisms						
Chlamydia pneumoniae		✔	✔	✔		
Chlamydia trachomatis						✔
Mycoplasma pneumoniae		✔	✔	✔		

Indications

The Food and Drug Administration (FDA)-approved indications for the quinolones are noted in Table 4. While agents within this therapeutic class may have demonstrated positive activity via in vitro trials, the clinical significance of this activity remains unknown until fully demonstrated in well-controlled, peer-reviewed in vivo clinical trials. As such, this review and the recommendations provided are based exclusively upon the results of such clinical trials.

Table 3. Food and Drug Administration (FDA)-Approved Indications[1-10]

Indication	Ciprofloxacin	Gemifloxacin	Levofloxacin	Moxifloxacin	Norfloxacin	Ofloxacin
Dermatological Infections						
Skin and skin-structure infections	✔ §		✔	✔		✔
Gastrointestinal Infections						
Infectious diarrhea	✔ §					
Genitourinary Infections						
Cystitis	✔ §					✔
Pelvic inflammatory disease						✔
Prostatitis	✔ §		✔		✔	✔
Pyelonephritis	✔ §,†		✔			
Urethritis/cervicitis (gonococcal)	✔ §				✔	✔
Urethritis/cervicitis (non-gonococcal)						✔
Urinary tract infections	✔ §,†		✔		✔	✔
Respiratory Infections						
Acute exacerbations of chronic bronchitis		✔	✔	✔		✔
Inhalation anthrax (post-exposure)	✔ §		✔			
Pneumonia (community-acquired)		✔	✔	✔		✔
Pneumonia (nosocomial)			✔			
Respiratory tract infections (lower)	✔ §					
Sinusitis	✔ §		✔	✔		
Miscellaneous Infections						
Bone and/or joint infections	✔ §					
Intra-abdominal infections	✔ §			✔		
Plague			✔			
Typhoid fever	✔ §					

§Immediate-release formulation.
†Extended-release formulation.

Pharmacokinetics

Table 4. Pharmacokinetics[1-7]

Generic Name	Bioavailability (%)	Protein Binding (%)	Metabolism (%)	Excretion (%)	Half-Life (hours)
Ciprofloxacin	60 to 80	20 to 40	Liver	Renal (30 to 57) Feces (20 to 35)	IR: 3 to 6 ER: 6 to 7
Gemifloxacin	71	60 to 70	Liver	Renal (36) Feces (61)	4 to 12
Levofloxacin	99	24 to 38	Liver	Renal (87) Feces (4)	6 to 8
Moxifloxacin	90	30 to 50	Liver (52)	Renal (20) Feces (25)	8 to 16
Norfloxacin	30 to 40	10 to 15	Liver	Renal (30) Feces (30)	3 to 4
Ofloxacin	90 to 98	20 to 32	Liver	Renal (65 to 80) Feces (4 to 8)	5 to 7.5

Clinical Trials

The quinolones have been shown to be effective and approved by the FDA to treat a variety of infections, including dermatologic, gastrointestinal, genitourinary, respiratory, as well as several miscellaneous infections.[1-10]

Clinical trials have demonstrated the safety and efficacy of second and third generation quinolones.[40-70] Kaushik et al evaluated azithromycin to ciprofloxacin for the treatment of cholerae in young children aged 2 to 12 years. There was a statistically significant difference in clinical cure favoring azithromycin compared to ciprofloxacin (relative risk [RR], 1.34; 95% confidence interval [CI], 1.16 to 1.54; P<0.001); however, there was not a significant difference in bacteriological success (RR, 1.05; 95% CI, 1.00 to 1.10; P=0.06).[40] Clinical trials have demonstrated comparable efficacy and safety profiles among the quinolones for the treatment of skin and soft-tissue infections, genitourinary infections, respiratory tract infections, and other miscellaneous infections.[40-70]

Table 5. Clinical Trials

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Gastrointestinal Infections				
Kaushik et al.[40] Ciprofloxacin 20 mg/kg as a single dose vs azithromycin 20 mg/kg as a single dose	OL, RCT Children 2 to 12 years of age with watery diarrhea for ≤24 hours and severe dehydration, who tested positive for Vibrio cholerae by hanging drop examination or culture of stool	N=180 3 days	Primary: Clinical success (resolution of diarrhea within 24 hours) and bacteriological success (cessation of excretion of Vibrio cholerae by day three) Secondary: Duration of diarrhea, duration of excretion of Vibrio cholerae in stool, fluid requirement, and proportion of children with clinical or bacteriological relapse	Primary: Clinical success was 94.5% with azithromycin compared to 70.7% with ciprofloxacin (RR, 1.34; 95% CI, 1.16 to 1.54; P<0.001). Bacteriological success was 100% with azithromycin compared to 95.5% with ciprofloxacin (RR, 1.05; 95% CI, 1.00 to 1.10; P=0.06). Secondary: Patients treated with azithromycin had a shorter duration of diarrhea compared to patients receiving ciprofloxacin (54.6 vs 71.5 hours, respectively; P<0.001). Patients receiving azithromycin had a lesser duration of excretion of Vibrio cholerae than patients receiving ciprofloxacin (34.6 vs 52.1 hours; P<0.001). The amount of IV fluid was significantly less among patients who received azithromycin compared to those who received ciprofloxacin (4,704.7 vs 3,491.1 mL; P<0.001). The proportion of children with bacteriological relapse was comparable in both groups (6.7% with azithromycin vs 2.2% with ciprofloxacin; P=0.16). None of the children in either group had a clinical relapse.
Dermatological Infections				
Nicodemo et al.[41] Ciprofloxacin 500 mg BID for 10 days vs levofloxacin 500 mg QD for seven days	DB, MC, RCT Adult patients with uncomplicated skin and skin structure infections	N=272 7 to 10 days	Primary: Clinical success rate (defined as cure or improvement in signs and symptoms) Secondary: Microbiological	Primary: Clinical success was achieved in 96.1% of those on levofloxacin and 93.5% on ciprofloxacin (95% CI, –8.4 to 3.3). Secondary: Eradication was achieved in 93.0% of those on levofloxacin and 89.7% on ciprofloxacin (95% CI, –11.7 to 5.1). An adverse event related to the study medication was reported in 8.9% of the patients on levofloxacin and 8.2% of patients taking ciprofloxacin.

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
			eradication rate	Discontinuation due to an adverse event occurred in five patients taking levofloxacin and two patients taking ciprofloxacin.
Nichols et al.[42] Ciprofloxacin 500 mg BID for 10 days vs levofloxacin 500 mg QD for seven days	MC, OL, RCT Adult patients with uncomplicated skin and skin structure infections	N=469 7 to 10 days	Primary: Clinical success rate (defined as cured or improvement in signs and symptoms) Secondary: Microbiological eradication rate by patient and by pathogen	Primary: Clinical success was achieved in 98% of those on levofloxacin and 94% on ciprofloxacin (95% CI, –7.7 to 0.7). Secondary: Eradication was achieved in 98% of those on levofloxacin and 89% on ciprofloxacin (95% CI, –14.5 to –2.7). The eradication rate of the most prevalent pathogen, Staphylococcus aureus, was 100% with levofloxacin and 87% with ciprofloxacin (95% CI, –20.2 to –5.1). The eradication rate of the second most prevalent pathogen, Streptococcus pyogenes, was 100% with levofloxacin and 90% with ciprofloxacin (95% CI, –26.7 to 6.7). An adverse event related to the study medication was reported in 6% of the patients on levofloxacin and 5% of patients taking ciprofloxacin.
Genitourinary Infections				
Sandberg et al[43] Ciprofloxacin 500 mg BID for seven days, followed by placebo for seven days vs ciprofloxacin 500 mg BID for 14 days	DB, MC, OL, PC, RCT Adult, non-pregnant female patients diagnosed with acute pyelonephritis	N=248 14 days	Primary: Clinical and bacteriological efficacy Secondary: Long-term cumulative efficacy	Primary: The cure rate for the ciprofloxacin seven-day treatment group was 97% (N=71/73) compared to 96% (N=80/83) for the 14-day treatment group. This showed statistical non-inferiority of the seven-day treatment group to the 14-day treatment group (-0.9; 90% CI, -6.5 to 4.8; P=0.004). Secondary: The cumulative efficacy rate for the ciprofloxacin seven-day treatment group was 93% (N=68/73) compared to 93% (N=78/84) for the 14-day treatment group. The seven-day treatment was shown to be non-inferior to the 14-day treatment (-0.3%; 90% CI, -7.4 to 7.2; P=0.015).
Fourcroy et al.[44] Ciprofloxacin immediate-release 250 mg BID for three days	DB, MC, RCT Adult female patients with uncomplicated	N=1,037 3 days	Primary: Bacteriological eradication rates defined as $<10^4$ CFU/mL at four to	Primary: Eradication at four to 11days was observed in 93.4% of patients on the extended-release formulation compared to 89.6% in the immediate-release formulation (95% CI, –0.99 to 8.59).

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
vs ciprofloxacin extended-release 500 mg QD for three days	urinary tract infections		11 days Secondary: Bacteriological eradication rates at 28 to 42 days and clinical cure rates at four to 11days and at 25 to 50 days after therapy	Secondary: Eradication at 28 to 42 days was observed in 82.4% of patients on the extended-release formulation compared to 83.2% in the immediate-release formulation (95% CI, –8.00 to 6.40). Clinical cure at four to 11 days was observed in 85.7% of patients on the extended-release formulation compared to 86.1% in the immediate-release formulation (95% CI, –6.37 to 5.57). Clinical cure at 28 to 42 days was observed in 75.7% of patients on the extended-release formulation compared to 78.8% in the immediate-release formulation (95% CI, –10.60 to 4.40). Adverse events were reported in 12.7% of patients on the extended-release formulation and 14.7% on the immediate-release formulation (P=not specified). Seven patients on the extended-release formulation and three patients on the immediate-release formulation withdrew due to an adverse event.
Talan et al.[45] Ciprofloxacin immediate-release 500 mg BID for 7 to 10 days vs ciprofloxacin extended-release 1,000 mg QD for 7 to 10 days	DB, MC, RCT Adult patients with complicated urinary tract infections or acute uncomplicated pyelonephritis	N=1,035 7 to 14 days	Primary: Bacteriological eradication rates (defined as $<10^4$ CFU/mL) and clinical cure rates at five to 11 days and at 28 to 42 days after therapy Secondary: Adverse events	Primary: Eradication at five to 11 days was observed in 89% of patients on the extended-release formulation compared to 85% in the immediate-release formulation (95% CI, –2.4 to 10.3). Eradication at 28 to 42 days was observed in 69.3% of patients on the extended-release formulation compared to 61.2% in the immediate-release formulation (95% CI, –0.8 to 18.6). Clinical cure at five to 11 days was observed in 97% of patients on the extended-release formulation compared to 94% in the immediate-release formulation (95% CI, –1.2 to 6.9). Clinical cure at 28 to 42 days was observed in 82.9% of patients on the extended-release formulation compared to 80.7% in the immediate-release formulation (95% CI, –5.4 to 10.4). Secondary: Drug-related adverse events were reported in 13.2% of patients on the

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
				extended-release formulation and 13.5% on the immediate-release formulation. The most commonly reported adverse reactions were nausea, diarrhea, vaginal moniliasis, headache and dizziness. Sixteen patients on the extended-release formulation and 12 on the immediate-release formulation withdrew due to an adverse event.
Henry et al.[56] Ciprofloxacin immediate-release 250 mg BID for three days vs ciprofloxacin extended-release 500 mg QD for three days	DB, MC, RCT Adult female patients with uncomplicated urinary tract infections	N=891 3 days	Primary: Bacteriological eradication rates (defined as $<10^4$ CFU/mL) and clinical cure rates at four to 11 days and at 25 to 50 days after therapy Secondary: Adverse events	Primary: Eradication at four to 11 days was observed in 94.5% of patients on the extended-release formulation compared to 93.7% in the immediate-release formulation (95% CI, –3.5 to 5.1). Eradication at 28 to 42 days was observed in 85.8% of patients on the extended-release formulation compared to 81.3% in the immediate-release formulation (95% CI, –1.9 to 12.2). Clinical cure at four to 11 days was observed in 95.5% of patients on the extended-release formulation compared to 92.7% in the immediate-release formulation (95% CI, –1.6 to 7). Clinical cure at 28 to 42 days was observed in 89.0% of patients on the extended-release formulation compared to 86.6% in the immediate-release formulation (95% CI, –3.1 to 8.8). Secondary: Drug-related adverse events were reported in 10.4% of patients on the extended-release formulation and 9.2% on the immediate-release formulation.
Richard et al.[57] Ciprofloxacin 500 mg BID vs levofloxacin 250 mg QD vs lomefloxacin 400 mg QD	MA Adult patients with acute uncomplicated pyelonephritis	N=186 (2 trials) 7 to 14 days	Primary: Eradication rates, defined as $<10^4$ CFU/mL at five to nine days Secondary: Clinical cure rate, defined as complete resolution of symptoms	Primary: Eradication was observed in 95% of the patients on levofloxacin, 94% in patients on ciprofloxacin, and 95% in patients on lomefloxacin. Secondary: Clinical cure was observed in 92% of the patients on levofloxacin, 88% in patients on ciprofloxacin, and 80% in patients on lomefloxacin. An adverse event related to the study medication was reported in 2% of the patients on levofloxacin, 8% of patients taking ciprofloxacin, and 5% of patients taking lomefloxacin. One patient taking lomefloxacin withdrew due to an adverse

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
				event.
Bundrick et al.[58] Ciprofloxacin 500 mg BID vs levofloxacin 500 mg QD	DB, MC, RCT Adult male patients with a history of chronic prostatitis	N=377 28 days	Primary: Clinical success and microbiological eradication rates Secondary: Adverse events	Primary: Clinical success was observed in 75.0% of patients taking levofloxacin and 72.8% of those taking ciprofloxacin (95% CI, –13.27 to 8.87). Eradication was observed in 75.0% of patients taking levofloxacin and 76.8% of those taking ciprofloxacin (95% CI, –8.98 to 12.58). Secondary: Drug-related adverse effects were reported in 44.2% of patients taking levofloxacin and 37.2% taking ciprofloxacin. The most frequently reported adverse reaction was gastrointestinal in nature.
Schaeffer et al.[49] Ciprofloxacin 500 mg BID vs norfloxacin 400 mg BID	OL, PRO, RCT Adult patients with complicated urinary tract infection	N=72 10 to 21 days	Primary: Clinical cure rates, defined as complete resolution of symptoms and eradication of the infecting organism(s) after two to four days and five to nine days of therapy Secondary: Not reported	Primary: Clinical cure rates were 72% for those on norfloxacin and 79% on ciprofloxacin (P=0.56). Secondary: Not reported
Auquer et al.[50] Ciprofloxacin 500 mg once vs norfloxacin 400 mg BID for three days	DB, MC, RCT Adult female patients with uncomplicated urinary tract infection	N=226 3 days	Primary: Clinical cure and bacterial eradication (defined as $<10^5$ CFU/mL of a gram-negative bacteria or $<10^4$ CFU/mL of a gram-positive bacteria) at day	Primary: After seven days of treatment, clinical cure were observed in 91.2% of patients on ciprofloxacin and 93.8% in patients on norfloxacin. After seven days of treatment, eradication was observed in 91.2% of patients on ciprofloxacin and 92.0% in patients on norfloxacin. Statistical analysis yielded significant results in favor of the hypothesis of equivalence between the two treatment groups (P=0.0062).

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
			seven Secondary: Not reported	Drug-related adverse effects were reported in 17 patients taking ciprofloxacin and 13 taking norfloxacin. The most frequently reported adverse reaction was gastrointestinal in nature. Secondary: Not reported
Zalmanovici et al[51] Nitrofurantoin vs SMX/TMP vs β-lactams (amoxicillin, cefadroxil, cefpodoxime pivmecillinam*) vs nalidixic acid vs fluoroquinolones (amifloxacin*, ciprofloxacin, norfloxacin, ofloxacin)	MA Outpatient women 16 to 65 years of age with uncomplicated UTI defined by the presence of urinary complaints (and the absence of upper UTI signs) and leukocyturia or bacteriuria	N=6,016 ≥3 days	Primary: Short-term symptomatic cure and long-term symptomatic cure Secondary: 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	Primary: 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 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). Secondary: 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. 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.

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
				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.
Hooton et al[52] Cefpodoxime 100 mg BID for 3 days vs ciprofloxacin 250 mg BID for 3 days	AC, DB, NI, RCT Women 18 to 55 years of age with acute cystitis (symptoms of dysuria, frequency, and/or urgency) and pyuria (white blood cell count≥8 cells/mm3), and received antimicrobial treatment and also had a positive urine culture (defined as 102 or more colony-forming units/mL of uropathogen).	N=300 30 days	Primary: Clinical cure rate at day 30 Secondary: Clinical and microbiological cure at the first follow-up visit and vaginal E. coli colonization at each follow-up visit	Primary: 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). 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 not seen among women who reported one or more UTIs in the year before enrollment (84 vs 80%, respectively). 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. Secondary: 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). 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. 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

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
				susceptible strain during the recurrent UTI. 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). 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). 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% 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.
Perea et al.[53] Ciprofloxacin 500 mg BID vs ofloxacin 200 mg BID	DB, RCT Adult patients with nongonococcal urethritis	N=95 7 days	Primary: Clinical cure rates, defined as lack of symptoms and fewer than five polymorphonuclear leukocytes in a Gram-stained urethral smear Secondary: Not reported	Primary: Clinical cure rates two weeks after treatment was observed in 75% of patients on ciprofloxacin and 74% of those on ofloxacin. Secondary: Not reported
Raz et al.[54] Ciprofloxacin 250 mg BID vs ofloxacin 200 mg BID	DB, MC, RCT Adult female patients with complicated lower urinary tract infection	N=465 7 days	Primary: Bacteriological success, defined as sterile urine culture at five to nine days	Primary: Bacteriological success at five to nine days was observed in 87.2% of the patients taking ofloxacin and 90.1% of patients taking ciprofloxacin (95% CI, –4.4 to 10.0). Secondary: Bacteriological success at 28 to 42 days was observed in 76.1% of the patients

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
			Secondary: Bacteriological success at 28 to 42 days and clinical resolution after five to nine days and at 28 to 42 days	taking ofloxacin and 77.1 % of patients taking ciprofloxacin (95% CI, –9.2 to 10.5). Clinical cure at five to nine days was observed in 97.2% of the patients taking ofloxacin and 97.2% of patients taking ciprofloxacin (95% CI, –3.8 to 3.9). Clinical cure at 28 to 42 days was observed in 87.3% of the patients taking ofloxacin and 87.4% of patients taking ciprofloxacin (95% CI, –8.1 to 7.4). Drug-related adverse effects were reported in 10.9% of the women taking ciprofloxacin and 13.4% taking ofloxacin. The most frequently reported adverse reaction was gastrointestinal in nature. Thirteen women on ciprofloxacin and 16 on ofloxacin withdrew from the study due to adverse effects.
McCarty et al.[55] SMX-TMP 800-160 mg BID for three days vs ciprofloxacin 100 mg BID for three days vs ofloxacin 200 mg BID for three days	MC, RCT Women ≥18 years of age with primary urinary tract infection, confirmed by a positive urine culture obtained within 48 hours of study onset, presenting with signs and symptoms of dysuria, pyuria, and urinary frequency for <10 days duration	N=688 Up to 6 weeks	Primary: Pathogen eradication rate, clinical response rate (resolution of symptoms), relapse rate, premature discontinuation, adverse events Secondary: Not reported	Primary: End-of-study evaluation revealed a lack of statistically significant difference in the pre-treatment pathogen eradication rate between the study groups. Pathogen eradication occurred in 94% of ciprofloxacin, 93% of SMX-TMP, and 97% of ofloxacin-treated patients. At the four to six week follow-up evaluation, recurrence rates were 11% in the ciprofloxacin, 16% in the SMX-TMP, and 13% in the ofloxacin-treated group. Clinical success at the end of therapy was 31% in the ciprofloxacin, 41% in the SMX-TMP, and 39% in the ofloxacin-treated group. The frequency of adverse effects was 93% in the ciprofloxacin, 95% in the SMX-TMP, and 96% in the ofloxacin-treated group (P=0.03). Premature discontinuation of the study drug due to side effects was more common in the SMX-TMP group, compared to the ciprofloxacin and ofloxacin groups (P=0.02). Secondary: Not reported
Heystek et al.[56]	DB, MC, RCT	N=434	Primary: Clinical success	Primary: Clinical success rates two to 14 days following treatment were 96.6% with

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Moxifloxacin 400 mg QD for 14 days vs doxycycline 100 mg BID for 14 days, metronidazole 400 mg TID for 14 days, ciprofloxacin 500 mg as a single dose	Women with uncomplicated pelvic inflammatory disease	14 days	two to 14 days posttreatment (clinical cure and improvement combined) Secondary: Clinical cure rate at two to 14 days posttreatment, clinical success rate at 21 to 35 days posttreatment (clinical failures at day two to 14 posttreatment carried forward for follow-up), bacteriological response	moxifloxacin and 98% with the comparator regimen in the per protocol population (95% CI -4.5 to 1.6) Clinical success rates were 77.0% with moxifloxacin and 76.7% with the comparator regimen in the intent to treat population (95% CI, -5.8 to 6.9). Moxifloxacin was found to be non-inferior to the comparator arm. Secondary: At two to 14 days posttreatment, clinical cure rates were 81.5% with moxifloxacin and 83.2% with the comparator regimen in the per protocol population (95% CI -9.2 to 5.1). Clinical cure rates were 64.7% with moxifloxacin and 65.0% with the comparator regimen in the intent to treat population (95% CI, -7.5 to 7.0). Clinical success rates 21 to 35 days following treatment were 93.8% with moxifloxacin and 91.3% with the comparator regimen in the per protocol population (95% CI -3.8 to 7.4). Clinical success rates were 60.1% with moxifloxacin and 56.8% with the comparator regimen in the intent to treat (95% CI, -5.8 to 9.1).
Judlin et al.[57] Moxifloxacin 400 mg QD for 14 days vs levofloxacin 500 mg QD and metronidazole 500 mg BID for 14 days All patients positive for *Neisseria gonorrhoeae* also received ceftriaxone 250 mg IM as a single dose.	DB, MC, RCT Women with uncomplicated pelvic inflammatory disease	N=460 6 weeks	Primary: Clinical cure at test of cure visit (seven to 14 days after last dose of study drug) in the per protocol population Secondary: Clinical response during therapy and at the four week follow-up, microbiological response at test of cure, safety	Primary: The clinical cure rate at the test of cure visit was 78.4% with moxifloxacin and 81.6% with levofloxacin-metronidazole (P=0.460). Moxifloxacin was found to be non-inferior to levofloxacin-metronidazole. Secondary: In the intent to treat analysis 56.6% of patients receiving moxifloxacin and 56.9% of patients receiving levofloxacin-metronidazole experienced adverse events. A total of 4% of patients receiving moxifloxacin and 5.2% of patients receiving levofloxacin-metronidazole experienced at least one drug-related adverse event that resulted in premature termination of the study drug.

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Ross et al.[58] Moxifloxacin 400 mg QD for 14 days vs ofloxacin 400 mg BID in combination with metronidazole 500 mg BID	DB, MC, RCT Women with uncomplicated pelvic inflammatory disease	N=741 14 days	Primary: Clinical resolution rates at five to 24 days post-therapy Secondary: Clinical resolution at 28 to 42 days post-therapy and bacteriological response at five to 24 days	Primary: Clinical resolution was observed in 90.2% of patients on moxifloxacin and 90.7% of patients on ofloxacin and metronidazole (95% CI, –5.7 to 4.0). Secondary: Clinical resolution at 28 to 42 days was observed in 85.8% of patients on moxifloxacin and 87.9% of patients on ofloxacin and metronidazole (95% CI, –8.0 to 3.1). Bacteriological response at 5 to 24 days was observed in 87.5% of patients on moxifloxacin and 82.1% of patients on ofloxacin and metronidazole (95% CI, –8.3 to 8.8). Significantly more patients taking ofloxacin and metronidazole reported a drug-related adverse event (30.9%) than those taking moxifloxacin (22.5%; P=0.01). Most commonly reported adverse events were gastrointestinal in nature. Withdrawals due to a drug-related adverse event occurred in 6.3% of patients receiving moxifloxacin compared to 5.0% in the ofloxacin/metronidazole group (P=0.41).
Boothby et al.[59] Moxifloxacin 400 mg QD for 14 days vs ofloxacin 400 mg BID and metronidazole 400 mg BID	RETRO Women with uncomplicated pelvic inflammatory disease	N=741 14 days	Primary: Clinical response (significant improvement or response, marginal improvement, or no change/worse) Secondary: Tolerability	Primary: There was no significant difference in clinical response rates with moxifloxacin compared to ofloxacin-metronidazole (significant improvement/resolved: 70 and 77%, respectively; marginal improvement: 11 and 3%, respectively; no change/worse: 18 and 20%; P=0.14). Secondary: For those patients who attended clinic for follow-up, adverse events occurred in 16% of patients receiving moxifloxacin and in 19% of patients receiving ofloxacin-metronidazole. Most were gastrointestinal in nature.
Rafalsky et al.[60] Quinolones (ciprofloxacin, ciprofloxacin extended-release, fleroxacin, gemifloxacin,	MA Women with uncomplicated acute cystitis	N=7,535 (11 Trials) Variable duration	Primary: Clinical response, bacteriological eradication, and clinical success (cure or improvement) and	Primary: For all primary endpoint measures in all 11 trials, there were no significant differences in clinical or microbiological efficacy between the quinolones. Secondary: Not reported

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
levofloxacin, norfloxacin, ofloxacin, pefloxacin, or rufloxacin)			bacteriological eradication Secondary: Not reported	
Respiratory Infections				
Nouira et al.[61] SMX-TMP 800-160 mg BID for 10 days vs ciprofloxacin 750 mg BID for 10 days	DB, RCT Patients ≥40 years of age with an acute exacerbation of COPD requiring mechanical ventilation	N=170 10 days	Primary: Hospital death and need for an additional course of antibiotics Secondary: Duration of mechanical ventilation, length of hospital stay, and exacerbation-free interval	Primary: Combined hospital death and additional antibiotic prescription rates were similar in the two groups (16.4 vs 15.3% in the SMX-TMP vs ciprofloxacin group; 95% CI, -9.8% to 12.0; P=0.832). During the study, 15 patients died in the hospital, eight (8.2%) in the SMX-TMP group and eight (9.4%) in the ciprofloxacin group (P>0.05). Secondary: The mean exacerbation-free interval was similar in both treatment groups (83 vs 79 days in the SMX-TMP vs ciprofloxacin group; P=0.41). Of 38 patients initially receiving noninvasive ventilation in the SMX-TMP group, 17 (45%) were secondarily intubated vs 13 (34%) in the ciprofloxacin group (P=0.347). The duration of mechanical ventilation and length of hospital stay were similar in the two study groups. Adverse events were minor and comparably distributed in both treatment groups.
Sethi et al.[62] Gemifloxacin 320 mg QD for five days vs levofloxacin 500 mg QD	DB, MC, RCT Patients >40 years of age with acute exacerbation of chronic bronchitis	N=360 5 days	Primary: Clinical success rate (defined as resolution or significant improvement of symptoms) at days 14 to 21	Primary: Clinical success at 14 to 21 days was observed in 88.2% of patients treated with gemifloxacin and 85.1% in those treated with levofloxacin (95% CI, –4.67 to 10.72). Secondary: Clinical success at nine to 11 days was observed in 97.5% of patients treated with gemifloxacin and 93.5% in those treated with levofloxacin (95% CI, –0.61 to

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
for seven days			Secondary: Clinical success rate at days nine to 11 and at 28 to 35 days, bacteriologic eradication rate at nine to 11, 14 to 21 and at 28 to 35 days	8.51). Clinical success at 28 to 35 days was observed in 83.7% of patients treated with gemifloxacin and 78.4% in those treated with levofloxacin (95% CI, –3.83 to 14.34). Eradication at nine to 11 days was observed in 87.5% of patients treated with gemifloxacin and 90.4% in those treated with levofloxacin. Eradication at 14 to 21 days was observed in 78.4% of patients treated with gemifloxacin and 85.7% in those treated with levofloxacin. Eradication at 28 to 35 days was observed in 77.8% of patients treated with gemifloxacin and 70.5% in those treated with levofloxacin. Adverse events were reported in 39.6% of patients taking gemifloxacin and 33.7% of patients taking levofloxacin. Withdrawals due to adverse events occurred in four patients on gemifloxacin and 10 patients taking levofloxacin.
Blasi et al.[63] Prulifloxacin 600 mg QD for seven days vs levofloxacin 500 mg QD for seven days	DB, MC, RCT Patients at least 40 years of age with severe COPD, smokers or ex-smokers with > 10 pack years, diagnosed with an acute exacerbation of chronic bronchitis	N=346 7 days	Primary: Clinical assessment at the test of cure visit Secondary: Clinical efficacy at visit four (six-week follow-up), clinical efficacy at visit five (six-month follow-up) and microbiological efficacy	Primary: At the test of cure visit, 92.5% (N=161/174) of patients treated with prulifloxacin in the intent to treat population were cured. 96.5% (N=166/172) of patients treated with levofloxacin in the intent to treat population were cured. The difference in the percentage of cured patients was -3.98 (95% CI, -8.76 to 0.79), which demonstrates non-inferiority of prulifloxacin to levofloxacin. Secondary: At visit four, patients cured by prulifloxacin had a treatment success rate of 96.8% (N=150/155), as defined by patients with mild relapse plus persistent resolution. Patients cured by levofloxacin had a treatment success rate of 98.1% (N=153/156) at visit four. At visit five, patients cured by prulifloxacin had a treatment success rate of 95.7% (N=135/141). Patients cured by levofloxacin had a treatment success rate of 98.6% (N=140/142) at visit five. Success rate for microbiological efficacy was defined as eradication plus presumed eradication. The success rate for patients treated with prulifloxacin was 83.3% (N=70/84) in the intent to treat population compared to 89.5% (N=68/76) in patients treated with levofloxacin.
Siempos et al.[64]	MA	N=7,405	Primary:	Primary:

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Quinolones vs amoxicillin/clavulanate vs macrolides	Patients >18 years old with acute bacterial exacerbation of chronic bronchitis	(19 RCT) 26 weeks	Treatment success, hospitalization, mortality, adverse events Secondary: Not reported	There was no difference regarding treatment success in intention-to-treat and clinically evaluable patients between macrolides and quinolones, amoxicillin-clavulanate and quinolones, or amoxicillin/clavulanate and macrolides. The treatment success in microbiologically evaluable patients was lower for macrolides compared to quinolones (OR, 0.47; 95% CI, 0.31 to 0.69). There was no difference in the need for hospitalization for patients treated with macrolides compared to patients treated with quinolones (OR, 1.37; 95% CI, 0.75 to 2.5). Data regarding need for hospitalization were only available in two trials comparing amoxicillin/clavulanate with quinolones, and in one trial comparing amoxicillin/clavulanate with macrolides. There was no difference in mortality between macrolide-treated patients with acute bacterial exacerbation of chronic bronchitis and those treated with quinolones (OR, 1.96; 95% CI 0.45to8.51). Data on mortality were provided in only two trials comparing amoxicillin-clavulanate with quinolones. Fewer quinolone-recipients experienced a recurrence of acute bacterial exacerbation of chronic bronchitis after resolution of the initial episode compared to macrolide-recipients during the 26-week period following therapy. Adverse effects in general were similar between macrolides and quinolones. Administration of amoxicillin/clavulanate was associated with more adverse effects than quinolones (OR, 1.36; 95% CI 1.01to1.85). Secondary: Not reported
Wilson et al[65] (MAESTRAL) Moxifloxacin 400 mg QD for five days vs	AC, DB, MC, NI, RCT Patients ≥60 years of age with acute exacerbation of COPD	N=1,056 8 weeks	Primary: Clinical failure eight weeks post-therapy in the per protocol population Secondary: Clinical response in	Primary: Moxifloxacin was noninferior to amoxicillin/clavulanic acid with respect to clinical failure rates at eight weeks post-therapy in the per protocol population (20.6% vs 22.0%; 95% CI, -5.89 to 3.83). The analysis of the intention to treat population also demonstrated non-inferiority (95% CI, -5.50 to 3.03) but did not demonstrate superiority. Secondary:

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
amoxicillin/clavulanic acid 875/125 mg BID for seven days			patients with positive sputum cultures and bacteriological outcomes, time to clinical failure	Clinical failure rates in patients with bacteria isolated at baseline were significantly lower in moxifloxacin versus amoxicillin/clavulanic acid-treated patients, showing a treatment difference of approximately 6% in favor of moxifloxacin in the per protocol population with 50/260 (19.2%) patients in the moxifloxacin compared to 68/261 (26.1%) patients in the amoxicillin/clavulanic acid (90% CI, −15.0 to −0.75; P=0.030). Failure rates for the intention to treat with pathogens populations were 62/ 327 (19.0%) for the moxifloxacin group compared to 85/335 (25.4%) in the amoxicillin/clavulanic acid group (95% CI, −13.9 to −1.44; P=0.016). In patients without bacteria isolated at baseline, clinical failure rates were similar between treatment groups (moxifloxacin, 76/350 [21.7%]; amoxicillin/clavulanic acid, 61/340 [17.9%]; P=0.120). In the ITT population, time to clinical failure was similar in both treatment arms (P=0.688). In the ITT with pathogens population, time to clinical failure was significantly longer for moxifloxacin compared to amoxicillin/clavulanic acid (P=0.015). Failure rates were similar at end of therapy (moxifloxacin, 27/327 [8.3%]; amoxicillin/clavulanic acid, 33/335 [9.9%], with an increasing divergence in favor of moxifloxacin at four weeks post-therapy (44/327 [13.5%] vs 64/335 [19.1%]) and eight weeks post-therapy (62/327 [19.0%] vs 85/335 (25.4%); P value not reported).
Yoon et al[66] Levofloxacin 500 mg QD for seven days vs Cefuroxime 250 or 500 mg BID for seven days (mild to moderate or severe exacerbation group, respectively)	MC, OL, PG, RCT South Korean patients ≥18 years of age with acute exacerbation of COPD	N=126 5 to 7 days	Primary: Clinical success (defined as cure or improved at second return visit) Secondary: Microbiologic efficacy	Primary: Clinical success was achieved in 90.4% of patients in the levofloxacin group and 90.6% of those in the cefuroxime group (95% CI, -9.40 to 10.9), thus showing non-inferiority of levofloxacin to cefuroxime. Secondary: Microbiologic efficacy rates were 85.7% in the levofloxacin group and 68.8% in the cefuroxime group, with no statistically significant difference (P=0.62).
Griffin et al.[68]	RETRO	N=39	Primary: Time to clinical	Primary: The mean time to clinical stability for the macrolide group was 5.1 and 4.3 days

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Levofloxacin vs azithromycin or clarithromycin	Patients with Legionella pneumonia	Variable duration	stability and length of hospital stay Secondary: Not reported	for the levofloxacin group (P=0.43). The mean length of hospital stay for the macrolide group was 12.7 and 8.9 days for the levofloxacin group (P=0.10). Secondary: Not reported
Miscellaneous Infections				
Noel et al.[68] Levofloxacin 10 mg/kg BID vs amoxicillin/clavulanate (amoxicillin 45 mg/kg) BID	MC, RCT, SB Children six months to five years of age with recurrent and/or persistent acute otitis media that was unchanged or worsened after ≥three days of treatment with an antimicrobial regimen used to treat acute otitis media	N=1,650 27 days	Primary: Clinical cure rates at visit three (two to five days post-therapy) Secondary: Clinical cure rate at visit four (10 to 17 days post therapy), clinical success (cured or improved) at visits three and four, safety	Primary: Clinical cure rates were 72.4% with levofloxacin and 69.9% with amoxicillin/clavulanate (95% CI, -7.37 to 2.46). Levofloxacin was found to be non-inferior to amoxicillin/clavulanate. Cure rates were similar among different age groups: ≤24 months: 68.9 vs 66.2%, respectively (95% CI, -9.36 to 4.03); >24 months: 76.9 vs 75.1%; respectively (95% CI, -8.94 to 5.28). Secondary: Clinical cure rates at visit four were 74.9% for levofloxacin and 73.9% for amoxicillin/clavulanate (95% CI, -5.55 to 3.54). Clinical success rates at visit three were 94.0% for levofloxacin and 90.8% for amoxicillin/clavulanate (95% CI, -6.02 to -0.29). Clinical success rates at visit four were 83.6% for levofloxacin and 80.4% for amoxicillin/clavulanate (95% CI, -7.18 to 0.81). There was no difference observed between treatments regarding frequency or type of adverse events. Most adverse events were mild or moderate in severity (97% levofloxacin; 96% amoxicillin/clavulanate) with diarrhea being the most frequent.
GIMEMA Infection Program[69] Ciprofloxacin 500 mg BID	MC, RCT, SB Patients ≥14 years of age with neutropenia	N=801 Mean 29 days	Primary: Number of patients with febrile episodes, the number of days	Primary: Significantly less patients on ciprofloxacin (34%) developed fevers than norfloxacin 25% (P=0.01). The number of days with a fever did not differ significantly between treatment

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
vs norfloxacin 400 mg BID	with hematologic malignancies or had bone marrow transplantation or chemotherapy-induced neutropenia expected to last >10 days		with a fever, the number of days parenteral antibiotics were used, interval to first febrile episode or infection, compliance, classification of febrile episodes or infection, discontinuation due to adverse reactions and mortality Secondary: Not reported	groups. Mean duration of parenteral antibiotic use was significantly shorter with ciprofloxacin (10.1 days) vs norfloxacin (12.0 days; P=0.02). The interval to first febrile episode was longer with ciprofloxacin (8.3 days) compared to norfloxacin (7.2 days; P=0.055). Patients with ciprofloxacin had a lower rate of microbiologically documented infections (17% vs 24%; P=0.058). Differences among other febrile classifications (clinically documented infection, fever of unknown origin, or bacteremia) were not significant. Compliance was >90% and comparable between treatment groups. Discontinuation due to adverse events occurred in 2% of patients on norfloxacin and 4% of patients on ciprofloxacin. The mortality rate during neutropenic episodes was 13% with norfloxacin and 14% with ciprofloxacin.
Arjyal et al.[70] Gatifloxacin 10 mg/kg QD for 7 days vs chloramphenicol 75 mg/kg/day in four divided doses for 14 days	OL, RCT Patients with uncomplicated enteric fever	N=853 6 months	Primary: Treatment failure Secondary: Fever clearance time, late relapse, and fecal carriage	Primary: There were 14 treatment failures in the chloramphenicol group and 12 treatment failures in the gatifloxacin group (HR, 0.86; 95% CI, 0.40 to 1.86; P=0.70). Secondary: The median time to fever clearance was 3.95 days in the chloramphenicol group and 3.90 in the gatifloxacin group (P=0.64). There was no significant difference between the treatment groups in relapses until day 31 (P=0.35) or day 62 (P=0.77). Only three of 148 patients receiving chloramphenicol and none of 154 patients receiving gatifloxacin were stool-culture-positive at the end of one month (P=0.12). At the end of three months, only one patient in the chloramphenicol group had a positive stool culture, and at six months no patients had a positive stool culture.

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
				In the chloramphenicol group, 25% of culture-positive patients experienced at least one adverse event. In the gatifloxacin group, 16.9% of culture-positive patients experienced at least one adverse event.

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[1-10]

Generic Name	Population and Precaution				
	Elderly/ Children	Renal Dysfunction	Hepatic Dysfunction	Pregnancy Category	Excreted in Breast Milk
Ciprofloxacin	No dosage adjustment required in the elderly. Safety and efficacy have not been established in children <1 (IR) or <18 (ER) years of age.	No dose adjustment is needed for creatinine clearance >50 mL/min. For creatinine clearance 30 to 50 mL/min, use 250 to 500 mg every 12 hours. For creatinine clearance 5 to 29 mL/min, use 250 to 500 mg every 18 hours. For patients on hemodialysis or peritoneal dialysis, use 250 to 500 mg every 24 hours (after dialysis).	No dosage adjustment required; use in acute hepatic insufficiency is unknown.	C	Yes
Gemifloxacin	No dosage adjustment required in the elderly. Safety and efficacy have not been established in children <18 years of age.	No dose adjustment is needed for creatinine clearance >40 mL/min. For creatinine clearance ≤40 mL/min or patients who are receiving hemodialysis or peritoneal dialysis, use 160 mg every 24 hours.	No dosage adjustment required.	C	Unknown; use with caution
Levofloxacin	No dosage adjustment required in the elderly. Safety and efficacy have not been established in children <6 months of age.	No dose adjustment is needed for creatinine clearance ≥50 mL/min. For creatinine clearance of 20 to 49 mL/min, 10 to 19 mL/min and for patients on hemodialysis or peritoneal dialysis;	No dosage adjustment required.	C	Unknown; use with caution.

Generic Name	Population and Precaution				
	Elderly/ Children	Renal Dysfunction	Hepatic Dysfunction	Pregnancy Category	Excreted in Breast Milk
		see package insert for specific recommendations.			
Moxifloxacin	No dosage adjustment required in the elderly. Safety and efficacy have not been established in children <18 years of age.	No dose adjustment is required.	No dose adjustment needed; use with caution due to QT prolongation.	C	Unknown; use with caution.
Norfloxacin	No dosage adjustment required in the elderly. Safety and efficacy have not been established in children <18 years of age.	No dose adjustment is needed for creatinine clearance >30 mL/min. For creatinine clearance ≤30 mL/min, use 400 mg every 24 hours.	Specific guidelines for dosage adjustments in patients with hepatic impairment are not available.	C	Unknown; use with caution.
Ofloxacin	No dosage adjustment required in the elderly. Safety and efficacy have not been established in children <18 years of age.	No dose adjustment is needed for creatinine clearance >50 mL/min. For creatinine clearance 20 to 50 mL/min, use the usual recommended unit dose every 24 hours. For creatinine clearance <20 mL/min, use half the usual recommended unit dose every 24 hours.	No dose adjustment required in mild or moderate hepatic impairment. For severe hepatic impairment, use a max dose of 400 mg/day.	C	Yes

Adverse Drug Events

Table 7. Adverse Drug Events (%)[1-10]

Adverse Event	Ciprofloxacin	Gemifloxacin	Levofloxacin	Moxifloxacin	Norfloxacin	Ofloxacin
Cardiovascular						
Angina pectoris	<1	-	-	0.1 to 1.0	-	-
Atrial fibrillation	-	-	-	0.1 to 1.0	-	-
Atrial flutter	<1	-	-	-	-	-
Bradycardia	-	-	-	0.1 to 1.0	-	-
Cardiac arrest	<1	-	0.1 to 1.0	0.1 to 1.0	0.1 to 0.2	<1
Cerebral thrombosis	<1	-	-	-	-	-
Congestive heart failure	-	-	-	0.1 to 1.0	-	-
Hypertension	<1	-	-	0.1 to 1.0	-	<1
Hypotension	<1	-	-	0.1 to 1.0	-	<1
Myocardial infarction	<1	-	-	-	-	-
Palpitations	<1	-	0.1 to 1.0	0.1 to 1.0	0.1 to 0.2	<1
QT prolongation	✔	-	✔	0.1 to 1.0	✔	-
Supraventricular tachycardia	-	✔	-	-	-	-
Syncope	<1	✔	0.1 to 1.0	0.1 to 1.0	-	<1
Tachycardia	<1	-	✔	0.1 to 1.0	-	-
Ventricular arrhythmia	-	-	0.1 to 1.0	✔	✔	-
Ventricular ectopy	<1	-	-	-	-	-
Ventricular tachycardia	-	-	0.1 to 1.0	✔	-	-
Central Nervous System						
Abnormal dreaming	-	-	0.1 to 1.0	-	-	<1
Abnormal gait	<1	-	0.1 to 1.0	✔	-	-
Agitation	✔	-	0.1 to 1.0	0.1 to 1.0	-	-
Anosmia	✔	-	✔	-	-	-
Anxiety	-	≤0.1	0.1 to 1.0	0.1 to 1.0	0.1 to 0.2	<1
Asthenia	-	≤0.1	-	0.1 to 1.0	0.3 to 1.3	<1
Ataxia	<1	-	-	-	-	-
Chills	<1	-	-	0.1 to 11	0.1 to 0.2	<1
Confusion	✔	✔	0.1 to 1.0	0.1 to 1.0	✔	<1
Delirium	✔	-	-	-	-	-
Depersonalization	<1	-	-	-	-	-
Depression	<1	✔	0.1 to 1.0	0.1 to 1.0	0.1 to 0.2	<1
Dizziness	<1	1.7	0.3 to 3.0	3	1.7 to 2.6	1 to 5
Drowsiness	<1	-	-	-	-	-
Encephalopathy	-	-	✔	-	-	-
Fatigue	-	<1	<1	0.1 to 1.0	<1	1 to 3
Fever	<1	-	✔	1.1	0.3 to 1.0	1 to 3

Adverse Event	Ciprofloxacin	Gemifloxacin	Levofloxacin	Moxifloxacin	Norfloxacin	Ofloxacin
Hallucinations	<1	✔	0.1 to 1.0	0.1 to 1.0	-	<1
Headache	<1	4.2	0.3 to 6.0	4.2	2.0 to 2.8	1 to 9
Hyperkinesias	-	-	0.1 to 1.0	-	-	-
Hypertonia	-	-	0.1 to 1.0	-	-	-
Insomnia	<1	<1	4	1.9	0.1 to 0.2	3 to 7
Irritability	<1	-	-	-	-	-
Lethargy	<1	-	<1	0.1 to 1.0	<1	1 to 3
Lightheadedness	<1	-	-	✔	-	-
Malaise	<1	-	<1	0.1 to 1.0	<1	1 to 3
Manic reaction	<1	-	-	-	-	-
Migraine	<1	-	-	-	-	-
Nightmares	<1	-	0.1 to 1.0	-	-	-
Paranoia	-	-	✔	-	-	-
Paresthesia	<1	✔	0.1 to 1.0	0.1 to 1.0	0.3 to 1.0	<1
Peripheral neuropathy	✔	✔	✔	✔	✔	✔
Phobia	<1	-	-	-	-	-
Psychotic reactions	<1	✔	✔	✔	✔	-
Restlessness	<1	-	-	0.1 to 1.0	-	<1
Seizures	<1	✔	0.1 to 1.0	✔	✔	<1
Sleep disorder	-	-	0.1 to 1.0	-	0.1 to 0.2	-
Somnolence	<1	<1	0.1 to 1.0	0.1 to 1.0	0.3 to 1.0	1 to 3
Suicide attempt or ideation	-	-	✔	-	-	-
Tinnitus	<1	-	✔	0.1 to 1.0	-	<1
Tremor	<1	≤0.1	0.1 to 1.0	0.1 to 1.0	✔	<1
Weakness	<1	-	-	-	-	-
Vertigo	-	≤0.1	0.1 to 1.0	0.1 to 1.0	-	<1
Dermatological						
Cutaneous candidiasis	<1	-	-	-	-	-
Dermatitis	-	<1	-	0.1 to 1.0	✔	-
Eczema	-	≤0.1	-	-	-	-
Erythema multiform	-	✔	✔	-	✔	-
Erythema nodosum	<1	-	-	-	-	-
Exfoliative dermatitis	-	-	-	-	✔	-
Flushing	<1	≤0.1	-	-	-	-
Hyperpigmentation	<1	-	-	-	-	-
Night sweats	-	-	-	0.1 to 1.0	-	-
Petechia	<1	-	-	-	-	-
Photosensitivity	<1	≤0.1	✔	✔	✔	✔
Pruritus	<1	<1	1	0.1 to 1.0	0.3 to 1.0	1 to 3

Adverse Event	Ciprofloxacin	Gemifloxacin	Levofloxacin	Moxifloxacin	Norfloxacin	Ofloxacin
Rash	1	3.5	1	0.1 to 1.0	0.3 to 1.0	1 to 3
Stevens-Johnson syndrome	✔	-	✔	✔	✔	-
Sweating	<1	-	-	0.1 to 1.0	0.3 to 1.0	<1
Toxic epidermal necrolysis	✔	-	✔	✔	✔	-
Urticaria	<1	<1	0.1 to 1.0	0.1 to 1.0	0.1 to 0.2	<1
Gastrointestinal						
Abdominal pain/discomfort	<1	2.2	≤2	1.5	0.3 to 1.6	1 to 3
Anorexia	<1	<1	0.1 to 1.0	0.1 to 1.0	0.3 to 1.0	-
Constipation	✔	<1	3	<1	0.3 to 1.0	1 to 3
Diarrhea	1.6	5	5	6	0.3 to 1.0	1 to 4
Dry mouth	<1	<1	<1	0.1 to 1.0	0.3 to 1.0	1 to 3
Dyspepsia	✔	<1	2	1	0.3 to 1.0	<1
Dysphagia	<1	-	-	-	-	-
Esophagitis	-	-	0.1 to 1.0	-	-	-
Flatulence	<1	<1	-	0.1 to 1.0	0.3 to 1.0	1 to 3
Gastritis	-	<1	0.1 to 1.0	-	-	-
Gastroenteritis	-	-	0.1 to 1.0	0.1 to 1.0	-	-
Gastroesophageal reflux disease	-	-	-	0.1 to 1.0	-	-
Gastrointestinal bleeding	<1	-	-	0.1 to 1.0	-	-
Glossitis	-	-	0.1 to 1.0	-	-	-
Intestinal perforation	<1	-	-	-	-	-
Nausea	2.5	3.7	0.6 to 7.0	6.9	2.6 to 4.2	3 to 10
Oral candidiasis	<1	≤0.1	1	0.1 to 1.0	-	-
Painful oral mucosa	<1	-	-	-	-	-
Pancreatitis	-	-	0.1 to 1.0	-	✔	-
Pseudomembranous colitis	✔	✔	0.1 to 1.0	-	✔	✔
Taste alterations	<1	<1	✔	0.1 to 1.0	0.1 to 0.2	-
Vomiting	1	1.6	0.5 to 3.0	2.4	0.3 to 1.0	1 to 4
Genitourinary						
Albuminuria	✔	-	-	-	1	≥1
Breast pain	<1	-	-	-	-	-
Candiduria	✔	-	-	-	✔	-
Crystalluria	✔	-	-	-	✔	-
Cylindruria	✔	-	-	-	-	-
Dysuria	-	-	-	0.1 to 1.0	-	<1
Genital irritation (pain or rash)	-	✔	-	-	-	<1
Genital moniliasis	-	<1	0.1 to 1.0	-	-	-
Glucosuria	-	-	-	-	✔	≥1

Adverse Event	Ciprofloxacin	Gemifloxacin	Levofloxacin	Moxifloxacin	Norfloxacin	Ofloxacin
Hematuria	✔	-	-	-	-	≥1
Interstitial nephritis	<1	-	✔	✔	✔	-
Nephritis	<1	-	-	-	-	-
Polyuria	<1	-	-	-	-	<1
Proteinuria	-	-	-	-	1	≥1
Pyuria	-	-	-	-	✔	≥1
Renal Failure	<1	✔	0.1 to 1.0	0.1 to 1.0	✔	-
Renal function abnormal (non-specific)	-	-	0.1 to 1.0	✔	-	-
Urethral bleeding	<1	-	-	-	-	-
Urinary retention	<1	-	-	-	-	<1
Urine abnormalities	-	≤0.1	-	-	-	-
Vaginitis	<1	<1	<2	<1	-	1 to 5
Hematologic						
Acidosis	<1	-	-	-	-	-
Agranulocytosis	✔	-	-	✔	-	-
Anemia	<0.1	≤0.1	0.1 to 1.0	-	-	≥1
Aplastic anemia	-	-	✔	-	-	-
Eosinophilia	0.6	≤0.1	✔	0.1 to 1.0	1.5	≥1
Granulocytopenia	-	≤0.1	0.1 to 1.0	-	-	-
Hematocrit decreased	<0.1	0.3	-	0.1 to 1.0	0.6	-
Hematocrit increased	-	0.1	-	-	-	-
Hemoglobin decreased	<1	0.2	-	0.1 to 1.0	0.6	-
Hemoglobin increased	-	0.1	-	-	-	-
Hemolytic anemia	-	-	✔	-	-	-
Leukocytosis	<0.1	-	<1	0.1 to 1.0	-	≥ 1
Leukopenia	0.4	<1	✔	0.1 to 1.0	1.3	≥1
Lymphocytosis	-	-	-	-	-	≥1
Monocytes increased	<0.1	-	-	-	-	-
Neutropenia	-	-	-	0.1 to 1.0	1	≥1
Neutrophils decreased	-	0.5	-	-	1.4	-
Neutrophils increased	-	0.5	-	≥2	-	-
Pancytopenia	0.1	-	✔	✔	-	-
Platelets decreased	0.1	0.2	-	-	1	-
Platelets increased	0.1	1	-	0.1 to 1.0	-	-
Prothrombin time increased	<1	✔	✔	0.1 to 1.0	-	-
Red blood cell decreased	-	0.1	-	≥2	-	-
Red blood cell increased	-	0.1	-	-	-	-
Thrombocytosis	<1	-	-	0.1 to 1.0	1	≥1

Adverse Event	Ciprofloxacin	Gemifloxacin	Levofloxacin	Moxifloxacin	Norfloxacin	Ofloxacin
Thrombocytopenia	<1	≤0.1	0.1 to 1.0	0.1 to 1.0	1	≥1
Hepatic						
Hepatic failure	✔	-	✔	✔	✔	-
Hepatic function abnormal	-	-	0.1 to 1.0	0.1 to 1.0	-	-
Hepatitis	<1	-	✔	✔	✔	-
Jaundice	<1	-	✔	✔	✔	-
Laboratory Abnormalities						
Albumin decreased	-	0.3	-	≥2	-	-
Alkaline phosphatase increased	0.8	<1	0.1 to 1.0	0.1 to 1.0	1.1	≥1
Alanine aminotransferase increased	1.9	1.7	-	1.1	1.4	≥1
Aspartate aminotransferase increased	1.7	1.3	-	1.1	1.4 to 1.6	≥1
Bilirubin abnormalities	0.3	≤0.1	-	0.1 to 1.0	-	-
Blood urea nitrogen increased	0.9	0.3	-	0.1 to 1.0	✔	≥1
Calcium decreased	-	0.1	-	≥2	-	-
Calcium increased	-	<0.1	-	-	-	-
Cholesterol increased	✔	-	-	-	-	-
Creatinine phosphokinase increased	-	0.7	✔	-	-	-
Gamma-glutamyl transferase increased	-	≤0.1	-	1.1	-	-
Glucose abnormalities	<1	-	2	-	-	≥1
Hyperglycemia	-	<1	0.1 to 1.0	0.1 to 1.0	-	≥1
Hyperkalemia	-	-	0.1 to 1.0	-	-	-
Hypoglycemia	<0.1	-	0.1 to 1.0	0.1 to 1.0	-	-
Hypokalemia	-	-	-	1	-	-
Lactate dehydrogenase increased	-	≤0.1	-	-	-	-
Lactic acid dehydrogenase increased	0.4	-	<1	0.1 to 1.0	✔	-
Liver enzymes increased	-	-	0.1 to 1.0	0.1 to 1.0	✔	-
Potassium alterations	✔	0.3	-	-	-	-
Serum amylase increased	<1	-	-	0.1 to 1.0	-	-
Serum creatinine increased	1.1	0.2	-	0.1 to 1.0	✔	≥1
Serum lipase increased	<1	-	-	0.1 to 1.0	-	-
Sodium decreased	-	0.2	-	-	-	-
Sodium increased	-	0.1	-	-	-	-
Total protein decreased	-	0.1	-	-	-	-

Adverse Event	Ciprofloxacin	Gemifloxacin	Levofloxacin	Moxifloxacin	Norfloxacin	Ofloxacin
Triglycerides increased	✔	-	-	0.1 to 1.0	-	-
Uric acid increased	<0.1	-	-	0.1 to 1.0	-	-
Musculoskeletal						
Achiness or myalgia	<1	≤0.1	0.1 to 1.0	0.1 to 1.0	✔	<1
Arthralgia or back pain	<1	≤0.1	0.1 to 1.0	0.1 to 1.0	0.3 to 1.0	<1
Joint stiffness	<1	-	-	-	-	-
Leg cramps	-	≤0.1	-	-	-	-
Muscle injury	-	-	✔	-	-	-
Muscle spasms	-	-	-	0.1 to 1.0	-	-
Neck or chest pain	<1	-	1	0.1 to 1.0	0.1 to 0.2	-
Rhabdomyolysis	-	-	✔	-	-	-
Skeletal pain	-	-	0.1 to 1.0	0.1 to 1.0	-	-
Tendinitis/tendon rupture	✔	✔	0.1 to 1.0	✔	-	-
Respiratory						
Bronchospasm	<1	-	-	0.1 to 1.0	-	-
Cough	-	-	-	-	-	<1
Dyspnea	<1	≤0.1	1	0.1 to 1.0	✔	-
Epistaxis	<1	-	0.1 to 1.0	-	-	<1
Hemoptysis	<1	-	-	-	-	-
Hiccough	<1	-	-	-	-	-
Laryngeal or pulmonary edema	<1	-	-	-	-	-
Pneumonia	-	≤0.1	-	-	-	-
Pneumonitis	-	-	✔	-	-	-
Pulmonary embolism	<1	-	-	-	-	-
Rhinorrhea	-	-	-	-	-	<1
Wheezing	-	-	-	0.1-1	-	-
Other						
Allergic reaction	<1	-	0.1 to 1.0	-	0.1 to 0.2	-
Anaphylactic reactions	✔	✔	✔	✔	✔	-
Angioedema	<1	-	✔	✔	✔	<1
Dehydration	-	-	-	0.1 to 1.0	-	-
Edema	<1	≤0.1	1	0.1 to 1.0	0.1 to 0.2	<1
Eye Pain	<1	-	-	-	-	-
Foot Pain	<1	-	-	-	-	-
Fungal Infection	-	<1	-	0.1 to 1.0	-	-
Gout	<1	-	-	-	-	-
Hearing loss	<1	-	-	-	✔	<1
Hemorrhage	-	✔	-	-	-	-

Adverse Event	Ciprofloxacin	Gemifloxacin	Levofloxacin	Moxifloxacin	Norfloxacin	Ofloxacin
Hypersensitivity	<1	✔	✔	✔	✔	✔
Injection site reaction	<1	-	1	0.1 to 1.0	-	-
Leukocytoclastic vasculitis	-	-	✔	-	-	<1
Lymphadenopathy	<1	-	-	-	-	-
Myasthenia gravis exacerbation	✔	✔	✔	✔	-	-
Multi-organ failure	-	-	✔	-	-	-
Pain	<1	≤0.1	-	0.1 to 1.0	-	<1
Pain in extremities	<1	-	-	0.1 to 1.0	-	<1
Pharyngitis	-	≤0.1	-	-	-	-
Phlebitis	<1	-	0.1 to 1.0	0.1 to 1.0	-	-
Serum sickness-like reaction	-	-	✔	-	-	-
Vasodilation	-	-	✔	-	-	<1
Visual disturbances	<1	≤0.1	✔	0.1 to 1.0	0.1 to 0.2	1 to 3

✔ Percent not specified.
- Event not reported.

Contraindications

Table 8. Contraindications[1-7]

Contraindications	Ciprofloxacin	Gemifloxacin	Levofloxacin	Moxifloxacin	Norfloxacin	Ofloxacin
Coadministration with tizanidine.	✔					
History of tendinitis or tendon rupture associated with use of a fluoroquinolone					✔	
Hypersensitivity to the active ingredient, fluoroquinolones or any component of the product.	✔	✔	✔	✔	✔	✔

Warnings/Precautions

Table 9. Warnings and Precautions[1-7]

Warnings/Precautions	Ciprofloxacin	Gemifloxacin	Levofloxacin	Moxifloxacin	Norfloxacin	Ofloxacin
Arthropathic effects in animals; lameness in immature dogs and erosions of cartilage of weight-bearing joints	✔	✔	✔	✔		✔
Blood glucose disturbances including symptomatic hyper- and hypo-glycemia; use caution in at risk patients			✔			
Central nervous system effects; convulsions, increased intracranial pressure, toxic psychosis, and others	✔	✔	✔	✔	✔	✔
Clostridium difficile-associated diarrhea	✔	✔	✔	✔	✔	✔
Coadministration of theophylline; serious and fatal reaction have been reported – cardiac arrest, seizure, status epilepticus and respiratory failure	✔					
Coadministration with drugs metabolized by CYP1A2 causes increased concentrations of coadministered drug	✔					
Drug resistant bacteria; unlikely to provide a benefit in the absence of a proven or strongly suspected bacterial infection and increases the risk of the development of resistant bacteria	✔	✔	✔	✔	✔	✔
Hemolytic reactions have rarely occurred in patients with latent or actual defects in glucose-6-phosphate dehydrogenase activity					✔	
Hepatic impairment; use with						✔

Warnings/Precautions	Ciprofloxacin	Gemifloxacin	Levofloxacin	Moxifloxacin	Norfloxacin	Ofloxacin
caution; elimination may be reduced						
Hepatotoxicity including necrosis and hepatic failure have been reported acutely (1 to 39 days)	✔					
Hepatotoxicity, severe including acute hepatitis and fatal events (<14 days, most before 6 days)			✔			
Hydration; maintain hydration to prevent formation of highly concentrated urine	✔	✔	✔		✔	✔
Hypersensitivity reactions; anaphylactics	✔	✔	✔	✔	✔	✔
Lactating women; safety and efficacy has not been established	✔	✔	✔	✔	✔	✔
Musculoskeletal disorders in pediatric patients; do not use in children less than 18 years of age	✔	✔	✔			
Myasthenia Gravis exacerbation; increased muscle weakness	✔	✔	✔	✔	✔	✔
Other serious and sometimes fatal reactions have been reported	✔	✔	✔	✔	✔	✔
Pediatric patients; safety and efficacy has not been established in patients <18 years of age		✔			✔	✔
Peripheral Neuropathy	✔	✔	✔	✔	✔	✔
Photosensitivity/Phototoxicity; avoid exposure to sunlight	✔	✔	✔	✔	✔	✔
Pregnant women; safety and effectiveness has not been established	✔	✔			✔	✔
QT interval prolongation; rare cases of torsade de pointes	✔	✔	✔	✔	✔	✔

Warnings/Precautions	Ciprofloxacin	Gemifloxacin	Levofloxacin	Moxifloxacin	Norfloxacin	Ofloxacin
have been reported – avoid use in at risk patients						
Rash; increased, especially with age <40, female gender, use of hormone replacement therapy and longer duration of therapy		✔				
Renal impairment; dose adjustment is required	✔	✔	✔		✔	✔
Syphilis; not effective in treating syphilis, when being treated for gonorrhea, a syphilis test is recommended at time of diagnosis – follow up test after three months	✔				✔	✔
Tendinopathy and tendon rupture; may require surgical repair	✔	✔	✔	✔	✔	✔

Black Box Warning for Cipro® (ciprofloxacin), Cipro XR® (ciprofloxacin ER), Factive® (gemifloxacin), Levaquin® (levofloxacin), Noroxin® (norfloxacin) and ofloxacin[1-7]

WARNING
Fluoroquinolones are associated with an increased risk of tendinitis and tendon rupture in all ages. This risk is further increased in older patients usually over 60 years of age, in patients taking corticosteroid drugs, and in patients with kidney, heart or lung transplants. Fluoroquinolones may exacerbate muscle weakness in persons with myasthenia gravis. Avoid fluoroquinolones in patients with known history of myasthenia gravis.

Drug Interactions

Table 10. Drug interactions[1-10]

Generic Name(s)	Interaction	Mechanism
Quinolones (ciprofloxacin, gemifloxacin, levofloxacin, moxifloxacin, norfloxacin, ofloxacin)	Antiarrhythmic agents	Both quinolones and antiarrhythmics can cause prolongation of the QT interval. Additive prolongation may occur.
Quinolones	Warfarin	The effect is an increased anticoagulant effect of warfarin. The

Generic Name(s)	Interaction	Mechanism
(ciprofloxacin, levofloxacin, moxifloxacin, norfloxacin, ofloxacin)		mechanism is unknown.
Quinolones (ciprofloxacin, levofloxacin, moxifloxacin)	Methadone	Methadone inhibits cardiac potassium channels and prolongs QT interval. This may become significant with larger doses and in combination with other drugs that also prolong QT interval.
Quinolones (ciprofloxacin, norfloxacin)	Theophylline	Inhibition of hepatic metabolism of theophylline leads to increased theophylline levels and toxicity can occur.
Quinolones (levofloxacin, moxifloxacin)	Butyrophenones	May cause additive QT interval prolongation.
Quinolones (levofloxacin, moxifloxacin)	Macrolides and ketolides	Pharmacologic effects of macrolides/ketolides and quinolones on the cardiac conduction system and QT interval may be additive.
Quinolones (levofloxacin, moxifloxacin)	Phenothiazines	The risk of life-threatening cardiac arrhythmias, including torsades de pointes, may be increased. The mechanism is unknown.
Quinolones (ciprofloxacin, levofloxacin)	Sulfonylureas	The hypoglycemic effect of sulfonylureas may be increased. The mechanism is unknown.
Quinolones (levofloxacin, moxifloxacin)	Arsenic	May cause additive QT interval prolongation.
Quinolones (levofloxacin, moxifloxacin)	Cisapride	The risk of cardiovascular side effects may be increased. The mechanism is unknown.
Quinolones (levofloxacin, moxifloxacin)	Halofantrine	May cause additive QT interval prolongation.
Quinolones (levofloxacin, moxifloxacin)	Maprotiline	May cause additive QT interval prolongation.
Quinolones (levofloxacin, moxifloxacin)	Nilotinib	May cause additive QT interval prolongation.
Quinolones (levofloxacin, moxifloxacin)	Pimozide	May cause additive QT interval prolongation.
Quinolones (levofloxacin, moxifloxacin)	Tacrolimus	May cause additive QT interval prolongation.
Quinolones (levofloxacin, moxifloxacin)	Toremifene	Pharmacologic effects of toremifene and quinolones on electrical conduction of the heart may be additive.
Quinolones (levofloxacin, moxifloxacin)	Vandetanib	May cause additive QT interval prolongation.
Quinolones	Ziprasidone	The risk of life-threatening cardiac arrhythmias, including

Generic Name(s)	Interaction	Mechanism
(levofloxacin, moxifloxacin)		torsades de pointes, may be increased. The mechanism is unknown.
Quinolones (ciprofloxacin)	Tizanidine	Quinolones may inhibit tizanidine metabolism (CYP1A2). Tizanidine plasma concentrations may be elevated, increasing the pharmacologic and adverse effects (e.g., dizziness, hypotension).
Quinolones (levofloxacin)	Chloroquine	May cause additive QT interval prolongation.
Quinolones (ciprofloxacin, gemifloxacin, levofloxacin, moxifloxacin, norfloxacin, ofloxacin)	Aluminum salts	Gastrointestinal absorption of quinolones may be decreased, resulting in decreased pharmacologic effects of quinolones. Reduced gastrointestinal acidity may be an additional mechanism.
Quinolones (ciprofloxacin, gemifloxacin, levofloxacin, moxifloxacin, norfloxacin, ofloxacin)	Calcium salts	Gastrointestinal absorption of quinolones may be decreased, resulting in decreased pharmacologic effects of quinolones.
Quinolones (ciprofloxacin, gemifloxacin, levofloxacin, moxifloxacin, norfloxacin, ofloxacin)	Corticosteroids	Adverse effects may be additive or synergistic. Drug-induced tendon rupture may be increased by corticosteroid coadministration, especially in those 60 years of age or greater.
Quinolones (ciprofloxacin, gemifloxacin, levofloxacin, moxifloxacin, norfloxacin, ofloxacin)	Iron salts	The formation of insoluble chelates with iron decreases gastrointestinal absorption of quinolones.
Quinolones (ciprofloxacin, gemifloxacin, levofloxacin, moxifloxacin, norfloxacin, ofloxacin)	Magnesium salts	The gastrointestinal absorption of quinolones may be decreased due to formation of poorly soluble chelates with magnesium. Reduced gastrointestinal acidity may be an additional mechanism.
Quinolones (ciprofloxacin, gemifloxacin, levofloxacin, moxifloxacin, norfloxacin, ofloxacin)	Nonsteroidal antiinflammatory drugs	Nonsteroidal antiinflammatory drugs may reduce the renal elimination of quinolones and increase the risk of central nervous system stimulation and seizures.
Quinolones (ciprofloxacin,	Ketorolac	Ketorolac may reduce the renal elimination of quinolones and increase the risk of central nervous system stimulation and

Generic Name(s)	Interaction	Mechanism
gemifloxacin, levofloxacin, moxifloxacin, norfloxacin, ofloxacin)		seizures.
Quinolones (ciprofloxacin, gemifloxacin, levofloxacin, moxifloxacin, norfloxacin, ofloxacin)	Sucralfate	The aluminum in sucralfate may complex with quinolones to decrease gastrointestinal absorption.
Quinolones (ciprofloxacin, gemifloxacin, norfloxacin)	Didanosine	The pharmacologic effects of quinolones may be decreased. The magnesium and aluminum cations in the buffers present in didanosine tablets decrease gastrointestinal absorption of quinolones via chelation.
Quinolones (ciprofloxacin, norfloxacin)	Caffeine	Inhibition of hepatic microsomal enzymes by quinolones may decrease the metabolic elimination of caffeine.
Quinolones (ciprofloxacin)	Hydantoins	Ciprofloxacin may decrease serum concentrations and pharmacologic effects of hydantoins, especially in elderly patients. The mechanism is unknown.
Quinolones (ciprofloxacin)	Clozapine	Inhibition of cytochrome P450 1A2 isoenzymes by ciprofloxacin may decrease the metabolic elimination of clozapine. This may increase clozapine blood levels, leading to increased risk of clozapine's adverse effects.
Quinolones (ciprofloxacin)	Duloxetine	Inhibition of cytochrome P450 1A2 by ciprofloxacin may decrease the metabolic elimination of duloxetine.
Quinolones (ciprofloxacin)	Methotrexate	Displacement of methotrexate from protein binding sites by ciprofloxacin may increase plasma concentrations of methotrexate.
Quinolones (norfloxacin)	Mycophenolate	Changes in gut flora due to combination antimicrobial therapy with norfloxacin oral and metronidazole may decrease the enterohepatic recirculation of mycophenolate mofetil oral thereby decreasing mycophenolate exposure.
Quinolones (ciprofloxacin)	Sevelamer	Decreased gastrointestinal absorption of ciprofloxacin is suspected.

Dosage and Administration

Table 11. Dosing and Administration[1-7]

Generic Name	Usual Adult Dose	Usual Pediatric Dose	Availability
Ciprofloxacin	Bone and joint infections (mild to moderate): Suspension, tablet immediate-release: 500 mg every 12 hours for ≥ four to six weeks Bone and joint infections (severe or complicated):	Inhalational anthrax (post-exposure) in patients one to 17 years of age: Suspension, tablet immediate-release: 15 mg/kg every 12 hours for 60 days; maximum, 500 mg/dose	Suspension: 250 mg/5 mL 500 mg/5 mL Tablet (extended-release): 500 mg 1,000 mg

Generic Name	Usual Adult Dose	Usual Pediatric Dose	Availability
	Suspension, tablet immediate-release: 750 mg every 12 hours for ≥ four to six weeks Urethritis/cervicitis (gonococcal): Suspension, tablet immediate-release: 250 mg in a single dose Infectious diarrhea: Suspension, tablet immediate-release: 500 mg every 12 hours for five to seven days Inhalational anthrax: Suspension, tablet immediate-release: 500 mg every 12 hours for 60 days Intra-abdominal infections: Suspension, tablet immediate-release: 500 mg every 12 hours for seven to 14 days Prostatitis: Suspension, tablet immediate-release: 500 mg every 12 hours for 28 days Pyelonephritis: Suspension, tablet immediate-release: 500 mg every 12 hours for seven days Tablet extended-release: 1,000 mg every 24 hours for seven days Respiratory tract infections (lower) (mild to moderate): Suspension, tablet immediate-release: 500 mg every 12 hours for seven to 14 days Respiratory tract infections (lower) (sever to complicated): Suspension, tablet immediate-release: 750 mg every 12 hours for	Urinary tract infections or pyelonephritis in patients one to 17 years of age: Suspension, tablet immediate-release: 10 to 20 mg/kg every 12 hours for 10 to 21 days; maximum, 750 mg/dose (not to be exceeded even in patients weighing >51 kg) No information is available on dosing adjustments in patients with moderate or severe renal insufficiency (creatinine clearance < 50 mL/min).	Tablet (immediate-release): 100 mg 250 mg 500 mg 750 mg

Generic Name	Usual Adult Dose	Usual Pediatric Dose	Availability
	seven to 14 days Sinusitis: Suspension, tablet immediate-release: 500 mg every 12 hours for 10 days Skin and skin-structure infections (mild to moderate): Suspension, tablet immediate-release: 500 mg every 12 hours for seven to 14 days Skin and skin-structure infections (severe/complicated): Suspension, tablet immediate-release: 750 mg every 12 hours for seven to 14 days Typhoid fever: Suspension, tablet immediate-release: 500 mg every 12 hours for 10 days Urinary tract infections (acute uncomplicated): Tablet extended-release: 500 mg every 24 hours for three days Suspension, tablet immediate-release: 250 mg every 12 hours for three days Urinary tract infections (mild/moderate): Suspension, tablet immediate-release: 250 mg every 12 hours for seven to 14 days Urinary tract infections (severe/ complicated): Tablet extended-release: 1,000 mg every 24 hours for seven to 14 days Suspension, tablet immediate-release: 500 mg every 12 hours for		

Generic Name	Usual Adult Dose	Usual Pediatric Dose	Availability
	seven to 14 days		
Gemifloxacin	Acute exacerbations of chronic bronchitis: Tablet: 320 mg once daily for five days Pneumonia (community-acquired): Tablet: 320 mg once daily for five to seven days	Safety and efficacy in children have not been established.	Tablet: 320 mg
Levofloxacin	Acute exacerbations of chronic bronchitis: Solution, tablet: 500 mg once daily for seven days Inhalational anthrax (post-exposure): Solution, tablet: 500 mg once daily for 60 days Pneumonia (community-acquired): Solution, tablet: 500 mg once daily for seven to 14 days or 750 mg once daily for five days Pneumonia (nosocomial): Solution, tablet: 750 mg once daily for seven to 14 days Prostatitis: Solution, tablet: 500 mg once daily for 28 days Pyelonephritis: Solution, tablet: 750 mg once daily for five days or 250 mg once daily for 10 days Sinusitis: Solution, tablet: 750 mg once daily for five days or 500 mg once daily for 10 to 14 days Skin and skin-structure infections (complicated): Solution, tablet: 750 mg once daily for seven to 14 days	Inhalational anthrax (post-exposure) for patients ≥6 months of age: Solution, tablet: >50 kg, 500 mg once daily for 60 days; <50 kg, 8 mg/kg every 12 hours for 60 days (maximum, 250 mg/dose) Plague for patients ≥6 months of age: Solution, tablet: >50 kg, 500 mg once daily for 60 days; <50 kg, 8 mg/kg every 12 hours for 60 days (maximum, 250 mg/dose)	Solution: 250 mg/10 mL Tablet: 250 mg 500 mg 750 mg

Generic Name	Usual Adult Dose	Usual Pediatric Dose	Availability
	Skin and skin-structure infections (uncomplicated): Solution, tablet: 500 mg once daily for seven to 10 days Urinary tract infections (complicated): Solution, tablet: 750 mg once daily for five days or 250 mg once daily for 10 days Urinary tract infections (uncomplicated): Solution, tablet: 250 mg once daily for three days		
Moxifloxacin	Acute exacerbations of chronic bronchitis: Tablet: 400 mg once daily for five days Intra-abdominal infections: Tablet: 400 mg once daily for five to 14 days Pneumonia (community-acquired): Tablet: 400 mg once daily for seven to 14 days Sinusitis: Tablet: 400 mg once daily for 10 days Skin and skin-structure infections (complicated): Tablet: 400 mg once daily for seven to 21 days Skin and skin-structure infections (complicated): Tablet: 400 mg once daily for seven days	Safety and efficacy in children have not been established.	Tablet: 400 mg
Norfloxacin	Prostatitis: Tablet: 400 mg every 12 hours for 28 days Urethritis/cervicitis (gonococcal):	Safety and efficacy in children have not been established.	Tablet: 400 mg

Generic Name	Usual Adult Dose	Usual Pediatric Dose	Availability
	Tablet: 800 mg in a single dose Urinary tract infections (complicated): Tablet: 400 mg every 12 hours for 10 to 21 days Urinary tract infections (complicated): Tablet: 400 mg every 12 hours for three to 10 days		
Ofloxacin	Acute exacerbations of chronic bronchitis: Tablet: 400 mg every 12 hours for 10 days Cystitis: Tablet: 200 mg every 12 hours for three to seven days Urethritis/cervicitis (gonococcal): Tablet: 400 mg in a single dose for one day Urethritis/cervicitis (non-gonococcal): Tablet: 300 mg every 12 hours for seven days Pelvic inflammatory disease: Tablet: 400 mg every 12 hours for 10 to 14 days Pneumonia (community-acquired): Tablet: 400 mg every 12 hours for 10 days Prostatitis: Tablet: 300 mg every 12 hours for six weeks Skin and skin-structure infections: Tablet: 400 mg every 12 hours for 10 days Urinary tract infections: Tablet: 200 mg every 12 hours for 10 days	Safety and efficacy in children have not been established.	Tablet: 200 mg 300 mg 400 mg

Clinical Guidelines

The clinical guidelines contained in Table 12 are summarized globally and are not limited to the role of the fluoroquinolones. 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	Recommendation(s)
European Society of Cardiology: **Guidelines on the Prevention, Diagnosis, and Treatment of Infective Endocarditis (2009)**[13]	• Antibiotic treatment of infective endocarditis due to oral streptococci and group D streptococci: o Penicillin-susceptible strains: ▪ Penicillin G, amoxicillin or ceftriaxone for four weeks. ▪ Penicillin G, amoxicillin, or ceftriaxone plus gentamicin or netilmicin for two weeks. ▪ Vancomycin for four weeks (in beta-lactam allergic patients). o Penicillin-resistant strains: ▪ Penicillin G or amoxicillin for four weeks plus gentamicin for two weeks. ▪ Vancomycin for four weeks plus gentamicin for two weeks (in beta-lactam allergic patients). • Antibiotic treatment of infective endocarditis due to *Staphylococcus* species: o Methicillin-susceptible strains (native valves): ▪ Flucloxacillin or oxacillin for four to six weeks plus gentamicin for three to five days. ▪ Vancomycin for four to six weeks plus gentamicin for three to five days (penicillin-allergic patients or methicillin-resistant staphylococci). o Methicillin-susceptible strains (prosthetic valves): ▪ Flucloxacillin or oxacillin for at least six weeks, rifampin for at least six weeks, and gentamicin for two weeks. ▪ Vancomycin for at least six weeks, rifampin for at least six weeks, and gentamicin for two weeks (penicillin-allergic patients or methicillin-resistant staphylococci). • Antibiotic treatment of infective endocarditis due to *Enterococcus* species: o Beta-lactam and gentamicin susceptible strains: ▪ Amoxicillin plus gentamicin for four to six weeks. ▪ Ampicillin plus gentamicin for four to six weeks. ▪ Vancomycin plus gentamicin for six weeks. • Antibiotic treatment of blood culture-negative infective endocarditis: o *Brucella* species: ▪ Doxycycline, cotrimoxazole, and rifampin for ≥3 months. o *Coxiella burnetii* (agent of Q fever): ▪ Doxycycline plus hydroxychloroquine for >18 months. ▪ Doxycycline plus quinolone for >18 months. o *Bartonella* species: ▪ Ceftriaxone or ampicillin intravenous. ▪ Doxycycline orally for six weeks plus gentamicin or netilmicin for three weeks. o *Legionella* species: ▪ Erythromycin intravenous for two weeks, then orally for

Clinical Guideline	Recommendation(s)
	four weeks plus rifampin or ciprofloxacin orally for six weeks. o *Mycoplasma* species: ▪ Newer fluoroquinolones for >6 months. o *Tropheryma whipplei* (agent of Whipple's disease): ▪ Penicillin G or streptomycin intravenous for two weeks, then cotrimoxazole orally for one year. ▪ Doxycycline plus hydroxychloroquine orally for ≥18 months. • Proposed antibiotic regimens for initial empirical treatment of infective endocarditis (before or without pathogen identification): o Native valves: ▪ Ampicillin/sulbactam intravenous or amoxicillin/clavulanate intravenous plus gentamicin intravenous for four to six weeks. ▪ Vancomycin intravenous, gentamicin intravenous, and ciprofloxacin orally for four to six weeks. o Prosthetic valves (early, <12 months post surgery): ▪ Vancomycin intravenous for six weeks, gentamicin intravenous for two weeks, and rifampin orally for two weeks. o Prosthetic valves (late, ≥12 months post surgery): ▪ Ampicillin/sulbactam intravenous or amoxicillin/clavulanate intravenous plus gentamicin intravenous for four to six weeks. ▪ Vancomycin intravenous, gentamicin intravenous, and ciprofloxacin orally for four to six weeks.
American Heart Association: **Infective Endocarditis: Diagnosis, Antimicrobial Therapy, and Management of Complications (2005)**[14]	• Therapy for native valve endocarditis caused by viridans group streptococci and *Streptococcus bovis*: o Penicillin-susceptible strains: ▪ Penicillin G or ceftriaxone for four weeks. ▪ Penicillin G or ceftriaxone plus gentamicin for two weeks. ▪ Vancomycin for four weeks (recommended only for patients unable to tolerate penicillin or ceftriaxone therapy). o Penicillin-resistant strains: ▪ Penicillin G or ceftriaxone for four weeks plus gentamicin for two weeks. ▪ Vancomycin for four weeks (recommended only for patients unable to tolerate penicillin or ceftriaxone therapy). • Therapy for endocarditis of prosthetic valves or other prosthetic material caused by viridans group streptococci and *Streptococcus bovis*: o Penicillin-susceptible strains: ▪ Penicillin G or ceftriaxone for six weeks with or without gentamicin for two weeks. ▪ Vancomycin for six weeks (recommended only for patients unable to tolerate penicillin or ceftriaxone therapy). o Penicillin-resistant strains: ▪ Penicillin G or ceftriaxone for six weeks plus gentamicin

Clinical Guideline	Recommendation(s)
	for six weeks. ▪ Vancomycin for six weeks (recommended only for patients unable to tolerate penicillin or ceftriaxone therapy). • Therapy for endocarditis caused by staphylococci in the absence of prosthetic materials: o Oxacillin-susceptible strains: ▪ Nafcillin or oxacillin for six weeks with the option of adding gentamicin for three to five days. ▪ For penicillin-allergic individuals: cefazolin for six weeks with the option of adding gentamicin for three to five days. o Oxacillin-resistant strains ▪ Vancomycin for six weeks. • Therapy for prosthetic valve endocarditis caused by staphylococci: o Oxacillin-susceptible strains: ▪ Nafcillin or oxacillin plus rifampin (for at least six weeks) and gentamicin (for two weeks). o Oxacillin-resistant strains: ▪ Vancomycin plus rifampin (for at least six weeks) and gentamicin (for two weeks). • Therapy for native valve or prosthetic valve enterococcal endocarditis: o Strains susceptible to penicillin, gentamicin, and vancomycin: ▪ Ampicillin or penicillin G plus gentamicin for four to six weeks. ▪ Vancomycin plus gentamicin for six weeks (vancomycin therapy recommended only for patients unable to tolerate penicillin or ceftriaxone therapy). o Strains susceptible to penicillin, streptomycin, and vancomycin and resistant to gentamicin: ▪ Ampicillin or penicillin G plus streptomycin for four to six weeks. ▪ Vancomycin plus streptomycin for six weeks (vancomycin therapy recommended only for patients unable to tolerate penicillin or ceftriaxone therapy). o Strains resistant to penicillin and susceptible to aminoglycosides and vancomycin: ▪ β-lactamase–producing strain: • Ampicillin/sulbactam plus gentamicin for six weeks. • Vancomycin plus gentamicin for six weeks (vancomycin therapy recommended only for patients unable to tolerate penicillin or ceftriaxone therapy). ▪ Intrinsic penicillin resistance: • Vancomycin plus gentamicin for six weeks. • Therapy for both native and prosthetic valve endocarditis caused by *Haemophilus* species *(Haemophilus parainfluenzae, Haemophilus aphrophilus, Haemophilus paraphrophilus), Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens,* and *Kingella* species microorganisms: o Ceftriaxone (cefotaxime or another third- or fourth-generation

Clinical Guideline	Recommendation(s)
	cephalosporin may be substituted) or ampicillin/sulbactam or ciprofloxacin for four to six weeks. Fluoroquinolone therapy recommended only for patients unable to tolerate cephalosporin and ampicillin therapy; levofloxacin, gatifloxacin, or moxifloxacin may be substituted. • Therapy for culture-negative endocarditis including *Bartonella* endocarditis: o Native valve: ▪ Ampicillin/sulbactam plus gentamicin for four to six weeks. ▪ Vancomycin plus gentamicin plus ciprofloxacin for four to six weeks (vancomycin therapy recommended only for patients unable to tolerate penicillins).
American College of Cardiology/American Heart Association: **2008 Focused Update Incorporated Into the American College of Cardiology/American Heart Association 2006 Guidelines for the Management of Patients With Valvular Heart Disease (2008)[15]** American College of Cardiology/American Heart Association: **Guideline for the Management of Patients With Valvular Heart Disease (2014)[16] (although a more current guideline more detailed information was included as part of the 2008 Focused update; as such both are summarized together)**	<u>Rheumatic fever prophylaxis</u> • Primary prevention of rheumatic heart disease: o Penicillin G benzathine intramuscular once or penicillin V orally for 10 days. o Erythromycin estolate or erythromycin ethylsuccinate orally for 10 days, or azithromycin orally for five days in patients who are allergic to penicillin. • Secondary prevention of rheumatic fever: o Penicillin G benzathine intramuscular every four weeks, or penicillin V orally twice daily, or sulfadiazine orally once daily. o Erythromycin orally twice daily for patients who are allergic to penicillin. <u>Endocarditis prophylaxis</u> • Prophylaxis against infective endocarditis is reasonable for the following patients at highest risk for adverse outcomes from infective endocarditis who undergo dental procedures that involve manipulation of either gingival tissue or the periapical region of teeth or perforation of the oral mucosa: o Patients with prosthetic cardiac valve or prosthetic material used for cardiac valve repair. o Patients with previous infective endocarditis. o Patients with congenital heart disease. o Cardiac transplant recipients with valve regurgitation due to a structurally abnormal valve. • Prophylaxis against infective endocarditis is not recommended for non-dental procedures (such as transesophageal echocardiogram, esophagogastroduodenoscopy, or colonoscopy) in the absence of active infection. • Regimens for dental procedures (single dose 30 to 60 minutes before procedure): o Oral: amoxicillin. o Unable to take oral medications: ampicillin, cefazolin or ceftriaxone. o Allergic to penicillin or ampicillin (oral): cephalexin, clindamycin, or azithromycin. o Allergic to penicillins or ampicillin and unable to take oral medication: cefazolin, ceftriaxone, or clindamycin. • Therapy of native valve endocarditis caused by highly penicillin-

Clinical Guideline	Recommendation(s)
	susceptible viridans group streptococci and *Streptococcus bovis:* o Penicillin G or ceftriaxone for four weeks. o Ceftriaxone plus gentamicin for two weeks. o Vancomycin for four weeks in patients allergic to penicillin. • Therapy of native valve endocarditis caused by strains of viridans group streptococci and *Streptococcus bovis* relatively resistant to penicillin: o Penicillin G or ceftriaxone for four weeks plus gentamicin for two weeks. o Vancomycin for four weeks in patients allergic to penicillin. • Therapy for native valve or prosthetic valve enterococcal endocarditis caused by strains susceptible to penicillin, gentamicin, and vancomycin: o Ampicillin for four to six weeks or penicillin G plus gentamicin for four to six weeks. o Vancomycin plus gentamicin for six weeks in patients allergic to penicillin. • Therapy for endocarditis caused by staphylococci in the absence of prosthetic materials: o Oxacillin-susceptible strains: ▪ Nafcillin or oxacillin for six weeks plus the optional addition of gentamicin for three to five days. ▪ Cefazolin for six weeks with the optional addition of gentamicin in patients allergic to penicillin. o Oxacillin-resistant strains: ▪ Vancomycin for six weeks. • Therapy for prosthetic valve endocarditis caused by staphylococci: o Oxacillin-susceptible strains: ▪ Nafcillin or oxacillin, rifampin, and gentamicin for ≥6 weeks. o Oxacillin-resistant strains: ▪ Vancomycin, rifampin, and gentamicin for ≥6 weeks. • Therapy for both native and prosthetic valve endocarditis caused by *Haemophilus* species *(Haemophilus parainfluenzae, Haemophilus aphrophilus, Haemophilus paraphrophilus), Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens,* and *Kingella* species microorganisms: o Ceftriaxone for four weeks. o Ampicillin/sulbactam for four weeks. o Ciprofloxacin for four weeks. • Therapy for culture-negative endocarditis including *Bartonella* endocarditis: o Native valve: ▪ Ampicillin/sulbactam plus gentamicin (or vancomycin for patients allergic to penicillin) plus ciprofloxacin for four to six weeks. o Prosthetic valve (early; ≤1 year): ▪ Vancomycin for six weeks, plus gentamicin for two weeks, plus cefepime for six weeks, plus rifampin for six weeks. o Prosthetic valve (late; >1 year): ▪ Suspected *Bartonella*, culture negative: • Ceftriaxone for six weeks plus gentamicin with/without doxycycline for six weeks.

Clinical Guideline	Recommendation(s)
	▪ Documented *Bartonella*, culture positive: • Doxycycline for six weeks plus gentamicin for two weeks.
Infectious Diseases Society of America: **Clinical Practice Guidelines: Management of Encephalitis (2008)[17] (Was reviewed and deemed current as of July 2011)**	Empirical therapy • Acyclovir should be initiated in all patients with suspected encephalitis, pending results of diagnostic studies. • Other empirical antimicrobial agents should be initiated on the basis of specific epidemiologic or clinical factors, including appropriate therapy for presumed bacterial meningitis, if clinically indicated. • In patients with clinical clues suggestive of rickettsial or ehrlichial infection during the appropriate season, doxycycline should be added to empirical treatment regimens. Bacteria • *Bartonella bacilliformis:* chloramphenicol, ciprofloxacin, doxycycline, ampicillin, or sulfamethoxazole/trimethoprim is recommended. • *Bartonella henselae:* doxycycline or azithromycin, with or without rifampin, can be considered. • *Listeria monocytogenes:* ampicillin plus gentamicin is recommended; sulfamethoxazole/trimethoprim is an alternative in the penicillin-allergic patient. • *Mycoplasma pneumoniae:* antimicrobial therapy (azithromycin, doxycycline, or a fluoroquinolone) can be considered. • *Tropheryma whipplei:* ceftriaxone, followed by either sulfamethoxazole/trimethoprim or cefixime, is recommended. Helminths • *Baylisascaris procyonis:* albendazole plus diethylcarbamazine can be considered; adjunctive corticosteroids should also be considered. • *Gnathostoma* species: albendazole or ivermectin is recommended. • *Taenia solium:* need for treatment should be individualized; albendazole and corticosteroids are recommended; praziquantel can be considered as an alternative. Rickettsioses and ehrlichiosis • *Anaplasma phagocytophilum:* doxycycline is recommended. • *Ehrlichia chaffeensis:* doxycycline is recommended. • *Rickettsia rickettsii:* doxycycline is recommended; chloramphenicol can be considered an alternative in selected clinical scenarios, such as pregnancy. • *Coxiella burnetii:* doxycycline plus a fluoroquinolone plus rifampin is recommended. Spirochetes • *Borrelia burgdorferi:* ceftriaxone, cefotaxime, or penicillin G is recommended. • *Treponema pallidum:* penicillin G is recommended; ceftriaxone is an alternative. Protozoa • *Acanthamoeba:* sulfamethoxazole/trimethoprim plus rifampin plus ketoconazole or fluconazole plus sulfadiazine plus pyrimethamine can

Clinical Guideline	Recommendation(s)
	be considered. • *Balamuthia mandrillaris:* pentamidine, combined with a macrolide (azithromycin or clarithromycin), fluconazole, sulfadiazine, flucytosine, and a phenothiazine can be considered. • *Naegleria fowleri:* amphotericin B (intravenous and intrathecal) and rifampin, combined with other agents, can be considered. • *Plasmodium falciparum:* quinine, quinidine, or artemether is recommended; atovaquone-proguanil is an alternative; exchange transfusion is recommended for patients with 110% parasitemia or cerebral malaria; corticosteroids are not recommended. • *Toxoplasma gondii:* pyrimethamine plus either sulfadiazine or clindamycin is recommended; sulfamethoxazole/trimethoprim alone and pyrimethamine plus atovaquone, clarithromycin, azithromycin, or dapsone are alternatives. • *Trypanosoma brucei gambiense:* eflornithine is recommended; melarsoprol is an alternative. • *Trypanosoma brucei rhodesiense:* melarsoprol is recommended.
European Federation of Neurological Societies: **Guideline on the Management of Community-acquired Bacterial Meningitis (2008)**[18]	Empirical therapy • Ceftriaxone 2 g every 12 to 24 hours or cefotaxime 2 g every six to eight hours. • Alternative therapy: meropenem 2 g every eight hours or chloramphenicol 1 g every six hours. • If penicillin or cephalosporin-resistant pneumococcus is suspected, use ceftriaxone or cefotaxime plus vancomycin 60 mg/kg every 24 hours after a loading dose of 15 mg/kg. • Ampicillin/amoxicillin 2 g every four hours if *Listeria* is suspected. Pathogen specific therapy • Penicillin-sensitive pneumococcal meningitis: o Benzyl penicillin 250,000 U/kg/day, ampicillin-amoxicillin 2 g every four hours, ceftriaxone 2 g every 12 hours or cefotaxime 2 g every six to eight hours. o Alternative therapy: meropenem 2 g every eight hours or vancomycin 60 mg/kg every 24 hours as a continuous infusion after a 15 mg/kg loading dose plus rifampicin 600 mg every 12 hours, or moxifloxacin 400 mg daily. • Pneumococcus with reduced susceptibility to penicillin or cephalosporins: o Ceftriaxone or cefotaxime plus vancomycin ± rifampicin. o Alternative therapy: moxifloxacin, meropenem or linezolid 600 mg combined with rifampicin. • Meningococcal meningitis: o Benzyl penicillin, ceftriaxone, or cefotaxime. o Alternative therapy: meropenem, chloramphenicol, or moxifloxacin. • *Haemophilus influenzae* type B: o Ceftriaxone or cefotaxime. o Alternative therapy: chloramphenicol–ampicillin-amoxicillin. • Listerial meningitis: o Ampicillin or amoxicillin 2 g every four hours ± gentamicin 1 to 2 mg every eight hours for the first seven to 10 days. o Alternative therapy: sulfamethoxazole/trimethoprim 10 to 20

Clinical Guideline	Recommendation(s)
	mg/kg every six to 12 hours or meropenem. • *Staphylococcal* species: o Flucloxacillin 2 g every four hours or vancomycin if penicillin allergy is suspected. o Rifampicin should also be considered in addition to either agent. Linezolid should be considered for methicillin-resistant staphylococcal meningitis. • Gram-negative *Enterobacteriaceae*: o Ceftriaxone, cefotaxime or meropenem. • Pseudomonal meningitis: o Meropenem ± gentamicin.
Infectious Diseases Society of America: **Practice Guidelines for the Management of Bacterial Meningitis (2004)**[19]	Empiric therapy • Empirical antimicrobial therapy is initiated either when the lumbar puncture is delayed or for patients with purulent meningitis and a negative cerebrospinal fluid gram stain result: o Age <1 month: ampicillin plus cefotaxime or ampicillin plus an aminoglycoside. o Age one to 23 months: vancomycin plus a third-generation cephalosporin. o Age two to 50 years: vancomycin plus a third-generation cephalosporin. o Age >50 years: vancomycin plus ampicillin plus a third-generation cephalosporin. o Basilar skull fracture: vancomycin plus a third-generation cephalosporin. o Penetrating head trauma: vancomycin plus cefepime, vancomycin plus ceftazidime, or vancomycin plus meropenem. o Post neurosurgery: vancomycin plus cefepime, vancomycin plus ceftazidime, or vancomycin plus meropenem. o Cerebrospinal fluid shunt: vancomycin plus cefepime, vancomycin plus ceftazidime, or vancomycin plus meropenem. Specific therapy • Recommendations for specific antimicrobial therapy in bacterial meningitis are based on isolated pathogens and susceptibility. • *Streptococcus pneumoniae* o Penicillin minimum inhibitory concentrations <0.1 µg/mL: standard therapy includes penicillin G or ampicillin; alternative therapies include ceftriaxone, cefotaxime, or chloramphenicol. o Penicillin minimum inhibitory concentrations 0.1 to 1.0 µg/mL: standard therapy includes ceftriaxone or cefotaxime; alternative therapies include cefepime or meropenem. o Penicillin minimum inhibitory concentrations ≥2 µg/mL: standard therapies include vancomycin plus ceftriaxone or cefotaxime; alternative therapies include gatifloxacin or moxifloxacin. o Cefotaxime or ceftriaxone minimum inhibitory concentrations ≥1.0 µg/mL: standard therapies include vancomycin plus ceftriaxone or cefotaxime (consider addition of rifampin if minimum inhibitory concentrations of ceftriaxone is >2 µg/mL); alternative therapies include gatifloxacin or moxifloxacin. • *Neisseria meningitides* o Penicillin minimum inhibitory concentrations <0.1 µg/mL:

Clinical Guideline	Recommendation(s)
	standard therapy includes penicillin G or ampicillin; alternative therapy includes ceftriaxone, cefotaxime or chloramphenicol. o Penicillin minimum inhibitory concentrations 0.1 to 1.0 µg/mL: standard therapy includes ceftriaxone or cefotaxime; alternative therapies include chloramphenicol, a fluoroquinolone or meropenem. • *Listeria monocytogenes* o Standard therapy includes ampicillin or penicillin G; alternative therapies include sulfamethoxazole/trimethoprim or meropenem. • *Streptococcus agalactiae* o Standard therapy includes ampicillin or penicillin G; alternative therapies include ceftriaxone or cefotaxime. • *Escherichia coli* and other Enterobacteriaceae o Standard therapy includes a third-generation cephalosporin; alternative therapies include aztreonam, fluoroquinolone, meropenem, sulfamethoxazole/trimethoprim or ampicillin. • *Pseudomonas aeruginosa* o Standard therapies include cefepime or ceftazidime; alternative therapies include aztreonam, ciprofloxacin, or meropenem (addition of an aminoglycoside should be considered). • *Haemophilus influenzae* β-lactamase negative strains o Standard therapy includes ampicillin; alternative therapies include ceftriaxone, cefotaxime, cefepime, chloramphenicol or a fluoroquinolone. • *Haemophilus influenzae* β-lactamase positive strains o Standard therapy includes a third-generation cephalosporin; alternative therapies include cefepime, chloramphenicol or a fluoroquinolone. • *Staphylococcus aureus* methicillin susceptible o Standard therapy includes nafcillin or ofloxacin; alternative therapies include vancomycin or meropenem. • *Staphylococcus aureus* methicillin resistant o Standard therapy includes vancomycin (consider addition of rifampin); alternative therapies include sulfamethoxazole/trimethoprim or linezolid. • *Staphylococcus epidermidis* o Standard therapy includes vancomycin (consider addition of rifampin); alternative therapy includes linezolid. • *Enterococcus* species ampicillin susceptible o Standard therapy includes ampicillin plus gentamicin. • *Enterococcus* species ampicillin resistant o Standard therapy includes vancomycin plus gentamicin. • *Enterococcus* species ampicillin and vancomycin resistant o Standard therapy includes linezolid.
Infectious Disease Society of America: **Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the**	Impetigo and ecthyma • 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. • Bullous and nonbullous impetigo can be treated with oral or topical antimicrobials, but oral therapy is recommended for patients with

Clinical Guideline	Recommendation(s)
Infectious Diseases Society of America (2014)[20]	numerous lesions or in outbreaks affecting several people to help decrease transmission of infection. Treatment for ecthyma should be an oral antimicrobial. o Treatment of bullous and nonbullous impetigo should be with either mupirocin or retapamulin twice daily for five days. 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. 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. o Systemic antimicrobials should be used for infections during outbreaks of poststreptococcal glomerulonephritis to help eliminate nephritogenic strains of *Streptococcus pyogenes* from the community. <u>Treatment for purulent skin and soft tissue infections (SSTIs) (cutaneous abscesses, furuncles, carbuncles, and inflamed epidermoid cysts)</u> • Gram stain and culture of pus from carbuncles and abscesses are recommended, but treatment without these studies is reasonable in typical cases. • Gram stain and culture of pus from inflamed epidermoid cysts are not recommended. • Incision and drainage is the recommended treatment for inflamed epidermoid cysts, carbuncles, abscesses, and large furuncles. • 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. <u>Recurrent skin abscesses</u> • 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. • Recurrent abscesses should be drained and cultured early in the course of infection. • After obtaining cultures of recurrent abscess, treat with a 5- to 10-day course of an antibiotic active against the pathogen isolated. • 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. • Adult patients should be evaluated for neutrophil disorders if recurrent

Clinical Guideline	Recommendation(s)
	abscesses began in early childhood. Erysipelas and cellulitis • Cultures of blood or cutaneous aspirates, biopsies, or swabs are not routinely recommended. • 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. • 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. • The recommended duration of antimicrobial therapy is five days, but treatment should be extended if the infection has not improved within this time period. • Elevation of the affected area and treatment of predisposing factors, such as edema or underlying cutaneous disorders, are recommended. • 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. • 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. • Systemic corticosteroids (e.g., prednisone 40 mg daily for seven days) could be considered in nondiabetic adult patients with cellulitis. Recurrent cellulitis • 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. • Administration of prophylactic antibiotics, such as oral penicillin or 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.

Clinical Guideline	Recommendation(s)
	Surgical site infections • Suture removal plus incision and drainage should be performed for surgical site infections. • 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. • 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. • 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. • 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. Necrotizing fasciitis, including Fournier gangrene • 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). • 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). • Penicillin plus clindamycin is recommended for treatment of documented group A streptococcal necrotizing fasciitis. Dog or cat bites • 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. • Postexposure prophylaxis for rabies may be indicated; consultation with local health officials is recommended to determine if vaccination should be initiated. Animal bite–related wounds • An antimicrobial agent or agents active against both aerobic and anaerobic bacteria such as amoxicillin/clavulanate should be used. • 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.

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	Erysipeloid • Penicillin or amoxicillin for 7 to 10 days is recommended for treatment of erysipeloid. Immunocompromised patients • 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. • Differential diagnosis for infection of skin lesions should include bacterial, fungal, viral, and parasitic agents. • 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]	• Empirical therapy should be based on the severity of the infection. • Current clinical data does not allow for the recommendation of any specific antibiotic regimen for diabetic foot infections. • Suggested agents are derived from available published clinical trials and expert experience. • Definitive regimens should consider results of culture and susceptibility tests, as well as the clinical response to the empirical regimen. Similar agents of the same drug class may be substituted. Some of these regimens may not have Food and Drug Administration approval for complicated skin and skin-structure infections, and only linezolid, ertapenem and piperacillin/tazobactam are currently specifically approved for diabetic foot infections. • Suggested empirical antibiotic regimens for mild infections: dicloxacillin, clindamycin, cephalexin, sulfamethoxazole/trimethoprim, amoxicillin/clavulanate, levofloxacin and doxycycline. • Suggested empirical antibiotic regimens for moderate infections: levofloxacin, cefoxitin, ceftriaxone, ampicillin/sulbactam, moxifloxacin, tigecycline, linezolid, daptomycin, ertapenem, ticarcillin/clavulanate, piperacillin/tazobactam, levofloxacin or ciprofloxacin with clindamycin, imipenem/cilastatin, vancomycin, ceftazidime, cefepime, aztreonam. • Suggested empirical antibiotic regimens for severe infections: piperacillin/tazobactam, vancomycin, ceftazidime, cefepime, aztreonam or a carbapenem.
World Gastroenterology Organization: **Acute Diarrhea (2012)**[22]	General considerations • Antimicrobials are the drugs of choice for empirical treatment of traveler's diarrhea and of community-acquired secretory diarrhea when the pathogen is known. • Consider antimicrobial treatment for: o *Shigella*, *Salmonella*, *Campylobacter* (dysenteric form), or parasitic infections. o Notyphoidal salmonellosis in at-risk populations (malnutrition, infants and elderly, immunocompromised patients and those with liver diseases and lymphoproliferative disorders) and in dysenteric presentation. o Moderate/severe traveler's diarrhea or diarrhea with fever

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	and/or with bloody stools. • Nitazoxanide may be appropriate for *Cryptosporidium* and other infections, including some bacteria. Antimicrobial agents for the treatment of specific causes of diarrhea • Cholera o First-line: doxycycline. o Alternative: azithromycin or ciprofloxacin. • Shigellosis o First-line: ciprofloxacin. o Alternative: pivmecillinam or ceftriaxone. • Amebiasis o First-line: metronidazole. • Giardiasis o First-line: metronidazole. o Alternative: tinidazole, omidazole or secnidazole. • *Campylobacter* o First-line: azithromycin. o Alternative: fluoroquinolones (e.g., ciprofloxacin).
Infectious Diseases Society of America: **The Practice of Travel Medicine (2006)**[23]	Chemoprophylaxis • Bismuth subsalicylate–containing formulations and antibiotics have been proven effective in preventing traveler's diarrhea. • Probiotics, such as lactobacillus, have not demonstrated sufficient efficacy to be recommended. • Widespread drug resistance renders doxycycline and sulfamethoxazole/trimethoprim no longer useful for prevention of traveler's diarrhea. • Chemoprophylaxis can contribute to development of resistant enteric bacteria and potentially predispose the traveler to infection with other deleterious pathogens, such as *Clostridium difficile.* • The routine use of antibiotic prophylaxis for travelers' diarrhea is not generally recommended. • Chemoprophylaxis may be considered in healthy travelers for whom staying well is critical and in special-needs travelers in whom the risk for diarrhea is increased or the consequences of a diarrheal episode may be severe. • When considering chemoprophylaxis, fluoroquinolone antibiotics remain the first choice. • Chemoprophylaxis should be recommended for no more than two to three weeks. Treatment • Fluid replacement and a diet restricted to liquids and bland foods may be appropriate, though they may not provide additional benefits beyond antibiotic treatment. • Symptomatic therapy with bismuth subsalicylate may be recommended in mild cases of diarrhea, but better agents exist for moderate-to-severe disease. • Loperamide has become the antimotility agent of choice. It is more efficacious in controlling diarrhea than bismuth subsalicylate and has an onset of action within the first four hours after ingestion. When it is used in combination with an antibiotic, there may be rapid improvement of

Clinical Guideline	Recommendation(s)
	traveler's diarrhea. • Antibiotics are effective in the treatment of traveler's diarrhea and can reduce the average duration of disease from several days to ~1 day. • Antibiotics that are recommended include fluoroquinolones (norfloxacin, ciprofloxacin, ofloxacin, levofloxacin), azithromycin, and rifaximin. • Fluoroquinolones remain predictably active for empiric therapy in most parts of the world and remain the drugs of first choice. • Antibiotics that are no longer recommended because of drug resistance worldwide are the sulfonamides, neomycin, ampicillin, doxycycline, tetracycline, trimethoprim alone, and sulfamethoxazole/trimethoprim.
Infectious Diseases Society of America: **Practice Guidelines for the Management of Infectious Diarrhea (2001)**[24]	Recommendations for therapy against specific pathogens • *Shigella* species: o Sulfamethoxazole/trimethoprim. o Fluoroquinolone. o Nalidixic acid. o Ceftriaxone. o Azithromycin. • *Salmonella,* non-typhi species: o Treatment is not routinely recommended; however, consider therapy in patients <6 months old or >50 years old, or patients that have a prosthesis, valvular heart disease, severe atherosclerosis, malignancy, or uremia. o Sulfamethoxazole-trimethoprim. o Fluoroquinolone. • *Campylobacter* species: o Erythromycin. • *Escherichia coli* species: o Sulfamethoxazole/trimethoprim. o Fluoroquinolone. • *Aeromonas* or *Plesiomonas* species: o Sulfamethoxazole/trimethoprim. o Fluoroquinolone • *Yersinia* species: o Antibiotic therapy is not usually required. For severe infections or associated bacteremia, combination therapy with doxycycline, aminoglycosides sulfamethoxazole/trimethoprim or a fluoroquinolone is recommended. • *Vibrio cholerae:* o Doxycycline or tetracycline. o Fluoroquinolone. • Toxigenic *Clostridium difficile:* o Metronidazole. • *Isospora* species: o Sulfamethoxazole/trimethoprim. • *Cyclospora* species: o Sulfamethoxazole/trimethoprim.
Centers for Disease Control and Prevention: **Sexually Transmitted Diseases Treatment Guidelines (2010)**[25]	Bacterial vaginosis • Recommended regimens: o Metronidazole 500 mg orally twice a day for seven days. o Metronidazole gel 0.75%, one full applicator (5 g) intravaginally, once a day for five days. o Clindamycin cream 2%, one full applicator (5 g) intravaginally at

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	bedtime for seven days. • Alternative regimens: o Tinidazole 2 g orally once daily for two days. o Tinidazole 1 g orally once daily for five days. o Clindamycin 300 mg orally twice daily for seven days. o Clindamycin ovules 100 mg intravaginally once at bedtime for three days. Cervicitis • Recommended regimens for presumptive treatment: o Azithromycin 1 g orally in a single dose. o Doxycycline 100 mg orally twice a day for seven days. Chancroid • Recommended regimens: o Azithromycin 1 g orally in a single dose. o Ceftriaxone 250 mg intramuscular in a single dose. o Ciprofloxacin 500 mg orally twice a day for three days. o Erythromycin base 500 mg orally three times a day for seven days. Chlamydial infections • Recommended regimens: o Azithromycin 1 g orally in a single dose. o Doxycycline 100 mg orally twice a day for seven days. • Alternative regimens: o Erythromycin base 500 mg orally four times a day for seven days. o Erythromycin ethylsuccinate 800 mg orally four times a day for seven days. o Levofloxacin 500 mg orally once daily for seven days. o Ofloxacin 300 mg orally twice a day for seven days. Chlamydial infections among children • Recommended regimen for children <45 kg: o Erythromycin base or ethylsuccinate 50 mg/kg/day orally divided into four doses daily for 14 days. • Recommended regimen for children ≥45 kg and <8 years of age: o Azithromycin 1 g orally in a single dose. • Recommended regimens for children ≥8 years of age: o Azithromycin 1 g orally in a single dose. o Doxycycline 100 mg orally twice a day for seven days. Disseminated gonococcal infection • Recommended regimen: o Ceftriaxone 1 g intramuscular or intravenous every 24 hours. • Alternative regimens: o Cefotaxime 1 g intravenous every eight hours. o Ceftizoxime 1 g intravenous every eight hours. Epididymitis • Recommended regimens :

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	o Ceftriaxone 250 mg intramuscular in a single dose plus doxycycline 100 mg orally twice a day for 10 days. • For acute epididymitis most likely caused by enteric organisms: o Levofloxacin 500 mg orally once daily for 10 days. o Ofloxacin 300 mg orally twice a day for 10 days. Granuloma inguinale (Donovanosis) • Recommended regimen: o Doxycycline 100 mg orally twice a day for at least three weeks and until all lesions have completely healed. • Alternative regimens: o Azithromycin 1 g orally once per week for at least three weeks and until all lesions have completely healed. o Ciprofloxacin 750 mg orally twice a day for at least three weeks and until all lesions have completely healed. o Erythromycin base 500 mg orally four times a day for at least three weeks and until all lesions have completely healed. o Sulfamethoxazole/trimethoprim one double-strength tablet orally twice a day for at least three weeks and until all lesions have completely healed. • The addition of an aminoglycoside (e.g., gentamicin 1 mg/kg intravenous every eight hours) to these regimens can be considered if improvement is not evident within the first few days of therapy. Gonococcal conjunctivitis • Recommended regimen: o Ceftriaxone 1 g intramuscular in a single dose. Gonococcal infections among children • Recommended regimen for children >45 kg: o Treat with one of the regimens recommended for adults. • Recommended regimen for children who weigh ≤45 kg and who have uncomplicated gonococcal vulvovaginitis, cervicitis, urethritis, pharyngitis, or proctitis: o Ceftriaxone 125 mg intramuscular in a single dose. • Recommended regimen for children who weigh ≤45 kg and who have bacteremia or arthritis: o Ceftriaxone 50 mg/kg (maximum dose: 1 g) intramuscular or intravenous in a single dose daily for seven days. • Recommended regimen for children who weigh >45 kg and who have bacteremia or arthritis: o Ceftriaxone 50 mg/kg intramuscular or intravenous in a single dose daily for seven days. Gonococcal meningitis and endocarditis • Recommended regimen: o Ceftriaxone 1 to 2 g intravenous every 12 hours. Lymphogranuloma venereum • Recommended regimen: o Doxycycline 100 mg orally twice a day for 21 days. • Alternative regimen:

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	o Erythromycin base 500 mg orally four times a day for 21 days. Nongonococcal urethritis • Recommended regimens: o Azithromycin 1 g orally in a single dose. o Doxycycline 100 mg orally twice a day for seven days. • Alternative regimens: o Erythromycin base 500 mg orally four times a day for seven days. o Erythromycin ethylsuccinate 800 mg orally four times a day for seven days. o Levofloxacin 500 mg orally once daily for seven days. o Ofloxacin 300 mg orally twice a day for seven days. Ophthalmia neonatorum caused by *Chlamydia trachomatis* • Recommended regimen: o Erythromycin base or ethylsuccinate 50 mg/kg/day orally divided into four doses daily for 14 days. Pelvic inflammatory disease • Recommended parenteral regimen A: o Cefotetan 2 g intravenous every 12 hours. o Cefoxitin 2 g intravenous every six hours plus doxycycline 100 mg orally or intravenous every 12 hours. • Recommended parenteral regimen B: o Clindamycin 900 mg intravenous every eight hours plus gentamicin loading dose intravenous or intramuscular (2 mg/kg of body weight), followed by a maintenance dose (1.5 mg/kg) every eight hours. Single daily dosing (3 to 5 mg/kg) can be substituted. • Alternative parenteral regimens: o Ampicillin/sulbactam 3 g intravenous every six hours plus doxycycline 100 mg orally or intravenous every 12 hours. • Recommended oral regimen: o Ceftriaxone 250 mg intramuscular in a single dose plus doxycycline 100 mg orally twice a day for 14 days with or without metronidazole 500 mg orally twice a day for 14 days. o Cefoxitin 2 g intramuscular in a single dose and probenecid, 1 g orally administered concurrently in a single dose, plus doxycycline 100 mg orally twice a day for 14 days with or without metronidazole 500 mg orally twice a day for 14 days. o Other parenteral third-generation cephalosporin (e.g., ceftizoxime or cefotaxime) plus doxycycline 100 mg orally twice a day for 14 days with or without metronidazole 500 mg orally twice a day for 14 days. Proctitis, proctocolitis, and enteritis • Recommended regimen: o Ceftriaxone 250 mg intramuscular plus doxycycline 100 mg orally twice a day for seven days. Recurrent and persistent urethritis

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	• Recommended regimens: o Metronidazole 2 g orally in a single dose. o Tinidazole 2 g orally in a single dose plus azithromycin 1 g orally in a single dose (if not used for initial episode). Primary and secondary syphilis • Recommended regimen for adults: o Benzathine penicillin G 2.4 million units intramuscular in a single dose. • Recommended regimen for infants and children: o Benzathine penicillin G 50,000 units/kg intramuscular, up to the adult dose of 2.4 million units in a single dose. Early latent syphilis • Recommended regimens for adults: o Benzathine penicillin G 2.4 million units intramuscular in a single dose. • Recommended regimens for children: o Benzathine penicillin G 50,000 units/kg intramuscular, up to the adult dose of 2.4 million units in a single dose. Late latent syphilis or latent syphilis of unknown duration • Recommended regimens for adults: o Benzathine penicillin G 7.2 million units total, administered as three doses of 2.4 million units intramuscular each at one-week intervals. • Recommended regimens for children: o Benzathine penicillin G 50,000 units/kg intramuscular, up to the adult dose of 2.4 million units, administered as three doses at one-week intervals. Tertiary syphilis • Recommended regimen: o Benzathine penicillin G 7.2 million units total, administered as three doses of 2.4 million units intramuscular each at one-week intervals. Neurosyphilis • Recommended regimen: o Aqueous crystalline penicillin G 18 to 24 million units per day, administered as 3 to 4 million units intravenous every four hours or continuous infusion, for 10 to 14 days. • Alternative regimen: o Procaine penicillin 2.4 million units intramuscular once daily plus probenecid 500 mg orally four times a day, both for 10 to 14 days. Uncomplicated gonococcal infections of the cervix, urethra, and rectum • Recommended regimens: o Ceftriaxone 250 mg intramuscular in a single dose. o Cefixime 400 mg orally in a single dose. o Single-dose injectable cephalosporin regimens plus

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	azithromycin 1g orally in a single dose or doxycycline 100 mg orally twice a day for seven days. Uncomplicated gonococcal infections of the pharynx • Recommended regimens: o Ceftriaxone 250 mg intermuscular in a single dose plus azithromycin 1g orally in a single dose or doxycycline 100 mg orally twice a day for seven days.
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 (2010)**[26]	Acute uncomplicated bacterial cystitis • Nitrofurantoin monohydrate/macrocrystals (100 mg twice daily for five days) is an appropriate choice for therapy due to minimal resistance and propensity for collateral damage. • Sulfamethoxazole/trimethoprim (800/160 mg twice daily for three days) is an appropriate choice for therapy, given its efficacy as assessed in numerous clinical trials, if local resistance rates of uropathogens causing acute uncomplicated cystitis do not exceed 20% or if the infecting strain is known to be susceptible. • Fosfomycin (3 g in a single dose) is an appropriate choice for therapy where it's available due to minimal resistance and propensity for collateral damage, but it appears to be less effective compared to standard short-course regimens. • Ofloxacin, ciprofloxacin and levofloxacin are highly efficacious in three-day regimens, but have a propensity for collateral damage and should be reserved for important uses other than acute cystitis and thus should be considered alternative antimicrobials for acute cystitis. • β-lactam agents, including amoxicillin/clavulanate, cefdinir, cefaclor, and cefpodoxime-proxetil, in three to seven day regimens are appropriate choices for therapy when other recommended agents cannot be used. Other β-lactams, such as cephalexin are less well studied, but may also be appropriate in certain settings. The β-lactams are generally less effective and have more adverse effects compared to other urinary tract infection antimicrobials. For these reasons, β-lactams should be used with caution for uncomplicated cystitis. • Amoxicillin or ampicillin should not be used for empirical treatment given the relatively poor efficacy and the very high prevalence of antimicrobial resistance to these agents worldwide. Acute pyelonephritis • Oral ciprofloxacin (500 mg twice daily) for seven days, with or without an initial 400 mg dose of intravenous ciprofloxacin, is an appropriate choice when resistance of community uropathogens to fluoroquinolones is not known to exceed 10%. A long-acting antimicrobial (i.e., ceftriaxone 1 g or consolidated 24 hour dose of an aminoglycoside) may replace the initial one time intravenous ciprofloxacin, and is recommended if the fluoroquinolone resistance is thought to exceed 10%. • Once-daily fluoroquinolones (ciprofloxacin 100 mg extended-release for seven days, levofloxacin 750 mg for five days) is an appropriate choice when resistance to community uropathogens is not known to exceed 10%. If resistance is thought to exceed 10%, an initial intravenous dose of long-acting parenteral antimicrobial (ceftriaxone 1 g or consolidated 24 hour dose of an aminoglycoside) is recommended. • Oral sulfamethoxazole/trimethoprim (800 to160 mg twice daily) for 14

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	days is an appropriate choice of therapy when the uropathogen is known to be susceptible. If susceptibility is unknown, an initial intravenous dose of long-acting parenteral antimicrobial (i.e., ceftriaxone 1 g or consolidated 24 hour dose of an aminoglycoside) is recommended. • Oral β-lactams are less effective than other available agents for the treatment of pyelonephritis. If an oral β-lactam is used, an initial intravenous dose of long-acting parenteral antimicrobial (i.e., ceftriaxone 1 g or consolidated 24 hour dose of an aminoglycoside) is recommended. • For patients requiring hospitalization, initial treatment with 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 is recommended. The choice between these agents should be based on local resistance data, and the regimen should be tailored on the basis of susceptibility results.
American College of Obstetricians and Gynecologists: **Treatment of Urinary Tract Infections in Nonpregnant Women (2008)**[27]	• Most urinary tract infections are caused by *E coli* (80 to 90%). • Other causes of urinary tract infections include *Staphylococcus saprophyticus*, *Proteus*, *Pseudomonas*, *Klebsiella* and *Enterobacter* species. • 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). • First generation cephalosporins and amoxicillin are less effective than the above agents due to resistance and rapid excretion from the urinary tract. • 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. • 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. • Sulfamethoxazole/trimethoprim is considered the preferred treatment for uncomplicated cystitis except in areas where resistance is common. • Fluoroquinolones should not be used first-line in areas where sulfamethoxazole/trimethoprim resistance is uncommon. • 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. • First-line treatment for pyelonephritis is now a fluoroquinolone. Sulfamethoxazole/trimethoprim may be used in areas of low resistance. o 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.
Working Group on Civilian Biodefense: **Anthrax as a Biological**	Inhalation anthrax in the contained casualty setting - adults • Ciprofloxacin 400 mg intravenous every 12 hours initially, then 500 mg by mouth twice daily when clinically appropriate; OR

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Weapon, Updated Recommendations for Management (2002)[28]	• Doxycycline 100 mg intravenous every 12 hours initially with either one or two of the following: rifampin, vancomycin, penicillin, ampicillin, chloramphenicol, imipenem, clindamycin, and/or clarithromycin. Switch to 100 mg by mouth twice daily when clinically appropriate. Inhalation anthrax in the contained casualty setting - children • Ciprofloxacin 10 to 15 mg/kg every 12 hours intravenous, then 10 to 15 mg/kg by mouth every 12 hours when clinically appropriate; OR • Doxycycline (if ≤45 kg to 2.2 mg/kg intravenous; if > 45 kg to100 mg intravenous) every 12 hours initially with either one or two of the following: rifampin, vancomycin, penicillin, ampicillin, chloramphenicol, imipenem, clindamycin, and/or clarithromycin. Switch to oral therapy when clinically appropriate using same intravenous dose. Inhalation anthrax in a mass casualty setting - adults • Recommended treatment: ciprofloxacin 500 mg by mouth every 12 hours. • Alternative treatment option: doxycycline 100 mg by mouth every 12 hours or amoxicillin 500 mg by mouth every eight hours. Inhalation anthrax in a mass casualty setting - children • Recommended treatment: ciprofloxacin 10 to 15 mg/kg by mouth every 12 hours. • Alternative treatment option: amoxicillin 500 mg by mouth every eight hours (weight ≥20 kg) or amoxicillin 40 mg/kg by mouth every eight hours (weight <20 kg). Inhalation anthrax in a mass casualty setting – pregnant women • Recommended treatment: ciprofloxacin 500 mg by mouth every 12 hours. • Alternative treatment option: amoxicillin 500 mg every eight hours.
Working Group on Civilian Biodefense: **Plague as a Biological Weapon: Medical and Public Health Management Consensus Statement (2000)**[29]	• For adults with pneumonic plague in the contained casualty settings, the preferred choice is streptomycin or gentamicin and alternative choices include doxycycline, ciprofloxacin, or chloramphenicol. • For children with pneumonic plague in the contained casualty settings, the preferred choice is streptomycin or gentamicin and alternative choices include doxycycline, ciprofloxacin, or chloramphenicol. • For pregnant women with pneumonic plague in the contained casualty settings, the preferred choice is gentamicin and an alternative choice is doxycycline. • For adults with pneumonic plague in the mass casualty setting and postexposure prophylaxis, the preferred choice is doxycycline, or ciprofloxacin and the alternative choice is chloramphenicol. • For children with pneumonic plague in the mass casualty setting and postexposure prophylaxis, the preferred choice is doxycycline or ciprofloxacin and an alternative choice is chloramphenicol. • For pregnant women with pneumonic plague in the mass casualty setting and postexposure prophylaxis, the preferred choice is doxycycline or ciprofloxacin and an alternative choice is chloramphenicol.
Global Initiative for Chronic Obstructive	• Prophylactic, continuous use of antibiotics has been shown to have no effect on the frequency of exacerbations in chronic obstructive

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Lung Disease: **Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease (2014)**[30]	pulmonary disease. • 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. • Based on current available evidence, antibiotics should be given to: o Patients with exacerbations of chronic obstructive pulmonary disease with the following three cardinal symptoms: dyspnea, sputum volume, and sputum purulence. 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. o Patients with a severe exacerbation of chronic obstructive pulmonary disease that requires mechanical ventilation (invasive or noninvasive). • The choice of antibiotic should be based on local bacterial resistance patterns. 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.
Infectious Diseases Society of America: **Management of Community-Acquired Pneumonia in Infants and Children Older Than 3 Months of Age (2011)**[31]	<u>Outpatient treatment</u> • 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. • 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*. • For patients allergic to amoxicillin, the following agents are considered alternative treatment options: o Second- or third-generation cephalosporin (cefpodoxime, cefuroxime, cefprozil). o Levofloxacin (oral therapy). o Linezolid (oral therapy). • 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. <u>Inpatient treatment</u> • 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*. • Empiric therapy with a third-generation parenteral cephalosporin (ceftriaxone or cefotaxime) should be prescribed for hospitalized infants

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	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. • 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. • 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. • 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*.
Infectious Diseases Society of America/American Thoracic Society: **Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults (2007)**[32]	Empirical antimicrobial therapy • Recommendations are generally for a class of antibiotics rather than for a specific drug, unless outcome data clearly favor one drug. • 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. • Outpatient treatment o Previously healthy and no risk factors for drug-resistant *Streptococcus pneumoniae* infection: ▪ Macrolide (azithromycin, clarithromycin, or erythromycin). ▪ Doxycycline. 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: ▪ Respiratory fluoroquinolone (moxifloxacin, gemifloxacin, or levofloxacin). ▪ 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). 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. • Inpatient, non-intensive care unit treatment o Respiratory fluoroquinolone. 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).

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	• Inpatient, intensive care unit treatment 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). o For *Pseudomonas* infection, use an antipneumococcal, antipseudomonal β-lactam (piperacillin/tazobactam, cefepime, imipenem, or meropenem) plus either ciprofloxacin or levofloxacin; OR o Antipneumococcal, antipseudomonal β-lactam (listed above) plus an aminoglycoside and azithromycin; OR 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). o For community-acquired methicillin-resistant *Staphylococcus aureus* infection, add vancomycin or linezolid.
American Family Physicians: **Diagnosis and Management of Community-Acquired Pneumonia in Adults (2011)**[33]	• Because the exact causative organism is not identified in many patients with community-acquired pneumonia, treatment is usually empiric. • Macrolides (e.g., azithromycin, clarithromycin, doxycycline) can be used for outpatients with no cardiopulmonary disease or recent antibiotic use. • 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): o A respiratory fluoroquinolone (levofloxacin, gemifloxacin, or moxifloxacin, or a beta-lactam antibiotic (high-dose amoxicillin, amoxicillin/clavulanate, or cefpodoxime) plus a macrolide. • Inpatients, non-intensive-care unit: o A respiratory fluoroquinolone, or a beta-lactam antibiotic plus a macrolide. • Inpatients, intensive care unit: o A beta-lactam antibiotic (ceftriaxone, cefotaxime, or ampicillin/sulbactam), plus azithromycin or a respiratory fluoroquinolone. • Risk factors for *Pseudomonas*: o A beta-lactam antibiotic (piperacillin/tazobactam, cefepime, imipenem/cilastatin, meropenem, or doripenem), plus either ciprofloxacin or levofloxacin OR o The above beta-lactam antibiotic plus an aminoglycoside and azithromycin OR o The above beta-lactam antibiotic plus an aminoglycoside and an antipneumococcal respiratory fluoroquinolone. • Risk factors for methicillin-resistant *Staphylococcus aureus:* o Vancomycin or linezolid. • Influenza virus: o Oseltamivir or zanamivir
American College of Chest Physicians: **Management of Community-Acquired Pneumonia in the**	• The oral route for medications is recommended if the patient can tolerate it, and if the availability and activity of the agents are adequate. • Severity of illness, patient age, comorbidities, concomitant medications, and ease of administration are all factors that can impact the empiric treatment decision.

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Home: An American College of Chest Physicians Clinical Position Statement (2005)[34]	• 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. • Amoxicillin/clavulanate and some second generation cephalosporins (cefuroxime, cefpodoxime, or cefprozil) are alternatives for low-risk patients. • 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. • 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 Thoracic Society/ Infectious Diseases Society of America: **Guidelines for the Management of Adults with Hospital-acquired, Ventilator-associated, and Healthcare-associated Pneumonia (2005)[35]**	• Select an initial empiric therapy based on the absence or presence of risk factors for multidrug-resistant pathogens. These risk factors include prolonged duration of hospitalization (five days or more), admission from a healthcare-related facility, and recent prolonged antibiotic therapy. • Patients with healthcare-related pneumonia should be treated for potentially drug-resistant organisms, regardless of when during the hospital stay the pneumonia begins. • In selecting empiric therapy for patients who have recently received an antibiotic, an effort should be made to use an agent from a different antibiotic class, because recent therapy increases the probability of inappropriate therapy and can predispose to resistance to that same class of antibiotics. • Initial empiric antibiotic therapy for hospital-acquired pneumonia or ventilator-associated pneumonia in patients with no known risk factors for multidrug-resistant pathogens, early onset, and any disease severity: o Ceftriaxone; OR o Levofloxacin, moxifloxacin, ciprofloxacin; OR o Ampicillin/sulbactam; OR o Ertapenem. • Initial empiric antibiotic therapy for hospital-acquired pneumonia, ventilator-associated pneumonia, and healthcare-associated pneumonia in patients with late-onset disease or risk factors for multidrug-resistant pathogens and all disease severity–combination antibiotic therapy is recommended as follows: o Antipseudomonal cephalosporin (cefepime, ceftazidime) or antipseudomonal carbapenem (imipenem or meropenem) or β-lactam-β-lactamase inhibitor (piperacillin/tazobactam) plus antipseudomonal fluoroquinolone (ciprofloxacin or levofloxacin) or aminoglycoside (amikacin, gentamicin, or tobramycin) plus linezolid or vancomycin if methicillin-resistant *Staphylococcus aureus* risk factors are present or there is a high incidence locally.
Infectious Diseases Society of America: **Diagnosis and Management of Complicated Intra-**	Community-acquired infection in adults: mild to moderate severity • Antibiotics selected should be active against enteric gram-negative aerobic and facultative bacilli, and enteric gram-positive streptococci. • Coverage for obligate anaerobic bacilli should be provided for distal small bowel, appendiceal, and colon-derived infection, and for more

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abdominal Infection in Adults and Children (2010)[36]	proximal gastrointestinal perforations in the presence of obstruction or paralytic ileus. • The use of ticarcillin/clavulanate, cefoxitin, ertapenem, moxifloxacin, or tigecycline as single-agent therapy or combinations of metronidazole with cefazolin, cefuroxime, ceftriaxone, cefotaxime, levofloxacin, or ciprofloxacin are preferable to regimens with substantial anti-*Pseudomonal* activity. • Because of increasing resistance, the following are not recommended for use (resistant bacteria also listed): Ampicillin/sulbactam (*Escherichia coli*), cefotetan and clindamycin (*Bacteroides fragilis*). • Aminoglycosides are not recommended for routine use due to availability of less toxic agents. • Empiric coverage for *Enterococcus* or antifungal therapy for *Candida* is not recommended in adults or children with community-acquired intra-abdominal infections. <u>Community-acquired infection in adults: high severity</u> • Antimicrobial regimens should be adjusted according to culture and susceptibility reports to ensure activity against the predominant pathogens isolated. Empiric use of antimicrobial regimens with broad-spectrum activity against gram-negative organisms, including meropenem, imipenem/cilastatin, doripenem, piperacillin/tazobactam, ciprofloxacin or levofloxacin in combination with metronidazole, or ceftazidime or cefepime in combination with metronidazole, is recommended. • Quinolone-resistant *Escherichia coli* have become common in some communities, and quinolones should not be used unless hospital surveys indicate >90% susceptibility of *Escherichia coli* to quinolones. • Aztreonam plus metronidazole is an alternative, but addition of an agent effective against gram-positive cocci is recommended. • In adults, routine use of an aminoglycoside or another second agent effective against gram-negative facultative and aerobic bacilli is not recommended in the absence of evidence that the patient is likely to harbor resistant organisms that require such therapy. • Empiric use of agents effective against enterococci is recommended. • Use of agents effective against methicillin-resistant Staphylococcus aureus or yeast is not recommended in the absence of evidence of infection due to such organisms. <u>Community-acquired infection in pediatric patients</u> • Selection of antimicrobial therapy should be based on origin of infection, severity of illness, and safety of the antimicrobial agents in specific pediatric age groups. • Acceptable broad spectrum agents include an aminoglycoside-based regimen, a carbapenem (imipenem, meropenem, or ertapenem), a β-lactam-β-lactamase-inhibitor combination (piperacillin/tazobactam or ticarcillin/clavulanate), or an advanced-generation cephalosporin (cefotaxime, ceftriaxone, ceftazidime, or cefepime) with metronidazole. It is not recommended in all patients with fever and abdominal pain if there is low suspicion of complicated appendicitis or other acute intra-abdominal infection. • Ciprofloxacin plus metronidazole or an aminoglycoside-based regimen,

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	are recommended for children with severe reactions to β-lactam antibiotics. • Fluid resuscitation, bowel decompression and broad-spectrum intravenous antibiotics should be used in neonates with necrotizing enterocolitis. These antibiotics include ampicillin, gentamicin, and metronidazole; ampicillin, cefotaxime, and metronidazole; or meropenem. Vancomycin may be used instead of ampicillin for suspected methicillin-resistant *Staphylococcus aureus* or ampicillin-resistant enterococcal infection. Fluconazole or amphotericin B should be used if the gram stain or cultures of specimens obtained at operation are consistent with a fungal infection. Health care-associated infection: • Therapy should be based on microbiologic results. To achieve empiric coverage, multi-drug regimens that include agents with expanded spectra of activity against gram-negative aerobic and facultative bacilli may be needed. These agents include meropenem, imipenem, imipenem/cilastatin, doripenem, piperacillin/tazobactam, or ceftazidime or cefepime in combination with metronidazole. Aminoglycosides or colistin may be required. • Broad spectrum therapy should be tailored upon microbiologic results to reduce number and spectra of administered agents. Cholecystitis and cholangitis: • Patients with suspected infection should receive antimicrobial therapy, but should have it discontinued within 24 hours after undergoing cholecystectomy unless evidence of infection outside the gallbladder wall.
Infectious Diseases Society of America: **Clinical Practice Guideline for the Use of Antimicrobial Agents in Neutropenic Patients with Cancer (2010)**[37]	Initial antibiotic therapy • Oral route: o For low-risk adults only; use ciprofloxacin plus amoxicillin/clavulanate. • Monotherapy with vancomycin not indicated: o Choose therapy with one of the following agents: cefepime or ceftazidime, or imipenem or meropenem. • Two drugs without vancomycin: o Choose an aminoglycoside plus antipseudomonal penicillin, cephalosporin (cefepime or ceftazidime), or carbapenem. • Vancomycin plus one or two antibiotics: o Choose cefepime or ceftazidime plus vancomycin, with or without an aminoglycoside; carbapenem plus vancomycin, with or without an aminoglycoside; or antipseudomonal penicillin plus an aminoglycoside and vancomycin. Modification of therapy during the first week of treatment • Patient becomes afebrile in three to five days: o Adjust therapy to the most appropriate drug(s). If no etiologic agent is identified and if the patient is at low risk initially, and oral antibiotic treatment was begun with no subsequent complications, continue use of the same drugs. o If the patient was at low risk initially and therapy with intravenous drugs was begun with no subsequent complications,

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	the regimen may be changed after 48 hours to oral ciprofloxacin plus amoxicillin/clavulanate for adults or cefixime for children. o If the patient is at high risk initially with no subsequent complications, continue use of the same intravenous drugs. • Persistent fever throughout the first three to five days: o Reassess therapy on day three. If there is no clinical worsening, continue use of the same antibiotics; stop vancomycin use if cultures do not yield organisms. o If there is progressive disease, change antibiotics. o If the patient is febrile after five days, consider adding an antifungal drug. Antibiotic prophylaxis for afebrile neutropenic patients • Use of antibiotic prophylaxis is not routine because of emerging antibiotic resistance, except for the use of sulfamethoxazole/trimethoprim to prevent *Pneumocystis carinii* pneumonitis.
National Comprehensive Cancer Network: **Prevention and Treatment of Cancer-Related Infections (2013)**[38]	Low infection risk prophylaxis • Antimicrobial prophylaxis is not recommended in patients with low infection risk. Intermediate infection risk prophylaxis • Consider using fluoroquinolone prophylaxis. High infection risk prophylaxis • Consider using fluoroquinolone prophylaxis. • Additional prophylaxis may be necessary. *Pneumocystis jirovecii* prophylaxis • Sulfamethoxazole/trimethoprim is highly effective for prophylaxis against *Pneumocystis jirovecii*. • Dapsone and pentamidine are potential alternatives as prophylaxis for patients intolerant to sulfamethoxazole/trimethoprim. • Atovaquone is another alternative for patients who are intolerant to sulfamethoxazole/trimethoprim. Bacterial infection prophylaxis with fluoroquinolone antibiotics • Fluoroquinolones are the most commonly used prophylactic antibiotics in adults with chemotherapy-induced neutropenia. • Fluoroquinolone prophylaxis should be considered in patients that have an expected duration of neutropenia longer than seven days. • Levofloxacin is the preferred prophylactic fluoroquinolone in neutropenic patients with cancer. • Ciprofloxacin: o Ciprofloxacin exerts good activity against gram-negative and atypical organisms. o Ciprofloxacin is not as effective as the “respiratory” fluoroquinolones against gram-positive organisms. o Ciprofloxacin has no activity against anaerobes. o If a patient has recently received fluoroquinolone prophylaxis, ciprofloxacin should be avoided as empiric treatment. o There is increasing resistance to ciprofloxacin in gram-negative

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	organisms at many treatment centers. • Levofloxacin: o Levofloxacin exerts good activity against gram-negative and atypical organisms. o Levofloxacin has improved activity against gram-positive organisms compared to ciprofloxacin. o Levofloxacin exerts limited activity against anaerobes. o Levofloxacin is recommended for prophylactic antibiotic treatment in neutropenic patients. Pneumococcal infection prophylaxis • Prophylaxis for pneumococcal infection should begin three months after patients undergo hematopoietic stem cell transplantation with penicillin, and prophylaxis should continue for at least one year after the transplant. • In regions that have pneumococcal isolates with intermediate or high-level resistance to penicillin, sulfamethoxazole/trimethoprim will likely be adequate for pneumococcal prophylaxis. Initial empiric antibiotic therapy • Patients with neutropenia should begin empiric treatment with broad spectrum antibiotics at the first sign of infection. • In certain low-risk patients, ciprofloxacin combined with amoxicillin/clavulanate is the oral regimen of choice for neutropenic fever treated in the outpatient setting. o Clindamycin may be used in place of amoxicillin/clavulanate for patients that are allergic to penicillin. o It is possible that quinolone monotherapy may be safe and effective for low-risk neutropenic fever; however, further study is needed before quinolone monotherapy can be routinely recommended. • Intravenous antibiotic monotherapy should be initiated with imipenem/cilastatin, piperacillin/tazobactam, or an extended-spectrum cephalosporin with antipseudomonal activity in patients with febrile neutropenia. • Empiric antibiotic therapy should be tailored to account for local susceptibilities or observed resistances on an institutional basis. • Aminoglycosides can be considered for empiric combination therapy with an antipseudomonal agent in complicated cases or cases involving resistant pathogens. • Empiric treatment with vancomycin should only be considered in patients at high risk for serious Gram-positive infections.
Surgical Infection Prevention Guideline Writers Workgroup: **Antimicrobial Prophylaxis for Surgery: An Advisory Statement from the National Surgical Infection Prevention Project**	General considerations • There is published evidence to support the use of many prophylactic antimicrobial regimens besides those included in this advisory statement or in existing guidelines. • Factors such as cost, half-life, safety, and antimicrobial resistance favor the use of older agents with a relatively narrow spectrum. • The use of newer, broad-spectrum drugs that are front-line therapeutic agents should be avoided in surgical prophylaxis to reduce emergence of bacterial strains that are resistant to these antimicrobials.

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(2004)[39]	Gynecologic and obstetrical surgery • For abdominal or vaginal hysterectomy, cefotetan is preferred, but reasonable alternatives are cefazolin and cefoxitin. In cases of β-lactam allergy, the workgroup recommends the use of one of the following regimens: clindamycin combined with gentamicin, aztreonam, or ciprofloxacin; metronidazole combined with gentamicin or ciprofloxacin; or clindamycin monotherapy. A single 750 mg dose of levofloxacin can be substituted for ciprofloxacin. • For cesarean section, a narrow-spectrum antimicrobial regimen similar to that recommended for hysterectomy provides adequate prophylaxis. Orthopedic total joint (hip and knee) arthroplasty • The preferred antimicrobials for prophylaxis in patients undergoing hip or knee arthroplasty are cefazolin and cefuroxime. • Vancomycin or clindamycin may be used in patients with serious allergy or adverse reactions to β-lactams. Cardiothoracic and vascular surgery • The recommended antimicrobials for cardiothoracic and vascular operations include cefazolin or cefuroxime. • For patients with serious allergy or adverse reaction to β-lactams, vancomycin is appropriate, and clindamycin may be an acceptable alternative. Colorectal surgery • Antimicrobial prophylaxis for colorectal operations can consist of an orally administered antimicrobial bowel preparation, a preoperative parenteral antimicrobial, or the combination of both. • Recommended oral prophylaxis consists of neomycin plus erythromycin or neomycin plus metronidazole, initiated no more than 18 to 24 hours before the operation, along with administration of a mechanical bowel preparation. • Cefotetan or cefoxitin are recommended for parenteral prophylaxis, and the combination of parenteral cefazolin and metronidazole is also recommended as an alternative. • For patients with confirmed allergy or adverse reaction to β-lactams, use of one of the following regimens is recommended: clindamycin combined with gentamicin, aztreonam, or ciprofloxacin; or metronidazole combined with gentamicin or ciprofloxacin. A single 750 mg dose of levofloxacin can be substituted for ciprofloxacin.

Conclusions

The second and third generation fluoroquinolones are valuable in treating a variety of infections, including dermatologic, gastrointestinal, genitourinary, respiratory, as well as several miscellaneous infections. Ciprofloxacin (Cipro®, Cipro XR®), levofloxacin (Levaquin®), norfloxacin (Noroxin®) and ofloxacin are considered second generation quinolones while gemifloxacin (Factive®) and moxifloxacin (Avelox®) are considered third generation quinolones. Differences are observed in microorganism susceptibilities. Norfloxacin, ciprofloxacin and ofloxacin have limited activity against streptococci and many anaerobes while levofloxacin and moxifloxacin have greater potency against gram-positive cocci, and moxifloxacin has enhanced activity against anaerobic bacteria. Gemifloxacin, levofloxacin and moxifloxacin are considered respiratory fluoroquinolones. They possess enhanced activity against *Streptococcus pneumoniae* while maintaining efficacy against *Haemophilus influenzae*, *Moraxella catarrhalis* and

atypical pathogens.[11-12] Clinical trials have demonstrated comparable efficacy and safety profiles among the quinolones for the treatment of skin and soft-tissue infections, genitourinary infections, respiratory tract infections, and other miscellaneous infections.[41-71]

Routes of elimination differ within the class. Ofloxacin and levofloxacin are eliminated mostly via the kidney, moxifloxacin is eliminated mostly via the liver, and the others are eliminated via a mix of kidney and liver.[11] Ciprofloxacin (immediate-release) and levofloxacin are the only medications approved for use in patients <18 years of age for certain indications. Ciprofloxacin may be used in patients >1 year of age and levofloxacin is approved for children >6 months of age.[1,4] Moxifloxacin is the only oral quinolone that does not need to adjusted in patients with renal disease.[5] All second and third generation quinolones are available in an oral tablet. Ciprofloxacin is also available in an extended-release tablet. Ciprofloxacin and levofloxacin are formulated as an oral suspension and solution respectively. In terms of dosing and administration, duration of therapy varies based on infection, but can be anywhere from several days to six weeks. Ciprofloxacin (extended-release), gemifloxacin, levofloxacin and moxifloxacin are approved for once daily dosing.[1-7] Ciprofloxacin, levofloxacin, moxifloxacin and ofloxacin are available in at least one generic formulation.

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