

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.¹⁻⁸ 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.^{9,10}

The quinolones are most active against gram-negative bacilli and gram-negative cocci.¹⁰ Ciprofloxacin has the most potent activity against gram-negative bacteria. 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.^{9,10} 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.^{9,10}

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.¹¹⁻³⁷

The fluoroquinolones have been the subject of several Food and Drug Administration (FDA) advisories which have included updates to their boxed warnings. The warnings now state that the benefits outweigh the risks in for serious bacterial infections, including anthrax, plague and bacterial pneumonia; however, their use in uncomplicated infections (e.g., acute bacterial sinusitis, acute exacerbation of chronic bronchitis and uncomplicated urinary tract infections) should be limited to when no other options are available.³⁸

This review excludes intravenous dosage forms and encompasses only the oral dosage forms.

Table 1. Medications Included Within the Therapeutic Class Review⁴⁻¹²

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	✓

Generic (Trade Name)	Food and Drug Administration Approved Indications	Dosage Form/Strength	Generic Availability
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	✓
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.³⁹⁻⁷¹
- 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).³⁹
- 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.³⁹⁻⁷⁰

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).¹¹⁻¹⁴
 - Use in prevention of infections after surgery in combination with other antibiotics.^{18,37}

- Recommend use of levofloxacin, moxifloxacin or levofloxacin/ciprofloxacin (in combination with clindamycin) for empiric therapy of diabetic foot infections.¹⁹
- First or second line in the treatment of infectious diarrhea, depending on specific cause.^{20,22}
- Quinolones are the first line for chemoprophylaxis and treatment of traveler's diarrhea.²¹
- Quinolones are first line or alternative therapies for sexually transmitted diseases such as chancroid, chlamydia, epididymitis and non-gonococcal urethritis.²³
- Second line for uncomplicated urinary tract infections and first line for acute pyonephritis.^{24,25}
- First line for inhalation anthrax; second line for plague^{26,27}
- Treatment for acute exacerbation of chronic obstructive pulmonary disease should be based on bacterial resistance patterns, but generally quinolones are not considered first line.²⁸
- 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.²⁹⁻³²
- 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.⁹
 - 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 be 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.¹⁻⁶
 - Ciprofloxacin (extended-release), gemifloxacin, levofloxacin and moxifloxacin are approved for once daily dosing.¹⁻⁷⁶
 - Ciprofloxacin, levofloxacin, moxifloxacin and ofloxacin are available in at least one generic formulation.

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