Fluoroquinolones, Oral
Therapeutic Class Review (TCR)

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FDA-APPROVED INDICATIONS

Drug	Manufacturer	Abdominal	AECB	Acute sinusitis	Bone and Joint	CAP	Nosocomial Pneumonia	Inhalational Anthrax	Infectious Diarrhea	Gonorrhea	LRTI	Febrile Neutropenia	PID	Plague	Prostatitis	Skin	Typhoid fever	UTI
ciprofloxacin* (Cipro®)[1]	generic, Bayer	X*	X	X	X	-	X	X	X	X	X	X	-	-	X	X	X	X
ciprofloxacin ER (Cipro XR®)[2]	generic, Bayer	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	X
delafloxacin† (Baxdela®)[3]	Melinta Therapeutics	-	-	-	-	X	-	-	-	-	-	-	-	-	-	X	-	-
gemifloxacin (Factive®)[4]	Vansen	-	X	-	-	X‡	-	-	-	-	-	-	-	-	-	-	-	-
levofloxacin (Levaquin®)[5]	generic, Janssen	-	X	X	-	X‡	X	X	-	-	-	-	-	X	X	X	-	X
moxifloxacin [6]	generic	X	X	X	-	X‡	-	-	-	-	-	-	-	-	-	X	-	-
ofloxacin[7]	generic	-	X	-	-	X§	-	-	-	X‖	-	-	X	-	X	X	-	X

Abdominal = Intra-abdominal infections, AECB = Acute exacerbation of chronic bronchitis, CAP = Community acquired pneumonia, LRTI = Lower respiratory tract infections, PID = Pelvic inflammatory disease, UTI = Urinary tract infection.

* Ciprofloxacin is indicated for complicated abdominal infections in combination with metronidazole and for complicated UTI and pyelonephritis caused by *Escherichia coli* in children ages 1 to 17 years; however, ciprofloxacin is not first line therapy for UTI or pyelonephritis. For nosocomial pneumonia and febrile neutropenia, ciprofloxacin (Cipro) IV, not oral, is indicated and should be used in combination with other agents.[8]

† Delafloxacin (Baxdela) is indicated for the treatment of acute bacterial skin and skin structure infections (ABSSSI) in adults caused by susceptible Gram-positive organisms (*Staphylococcus aureus* (including methicillin-resistant [MRSA] and methicillin-susceptible [MSSA] isolates), *Staphylococcus haemolyticus, Staphylococcus lugdunensis, Streptococcus agalactiae, Streptococcus anginosus* Group (including *Streptococcus anginosus, Streptococcus intermedius,* and *Streptococcus constellatus*), *Streptococcus pyogenes,* and *Enterococcus faecalis)* or Gram-negative organisms (*Escherichia coli, Enterobacter cloacae, Klebsiella pneumoniae,* and *Pseudomonas aeruginosa) and for the treatment of adults with community-acquired bacterial pneumonia (CABP) caused by designated susceptible bacteria*. It should be used only to treat infections that are proven or strongly suspected to be caused by susceptible bacteria to limit development of drug-resistant bacteria.

‡ Gemifloxacin (Factive), levofloxacin (Levaquin), and moxifloxacin are indicated for the treatment of CAP due to multi-drug resistant *Streptococcus pneumoniae*.

§ Ofloxacin is indicated for *Haemophilus influenza* and *Streptococcus pneumoniae* in CAP only.[9]

‖ Ofloxacin is also indicated for nongonococcal urethritis and cervicitis due to *Chlamydia trachomatis* and in mixed infections with *Chlamydia trachomatis* and *Neisseria gonorrhea*.

OVERVIEW

Oral fluoroquinolones vary in the spectrum of antimicrobial activity. The older fluoroquinolones have a gram-negative spectrum of activity and are useful in the treatment of urological infections. Newer fluoroquinolones have broad spectrums of activity covering both gram-negative and gram-positive bacteria, and some agents are useful in the treatment of penicillin-resistant *Streptococcus pneumoniae*. Culture and sensitivity information should guide antibiotic selection when available.

Levofloxacin (Levaquin) is indicated for the treatment of plague due to *Yersinia pestis* (*Y. pestis*), including pneumatic and septicemic plague, and for plague prophylaxis following exposure in adults and pediatrics, 6 months of age and older.[10] It joins streptomycin, doxycycline, tetracycline, and other antibacterials in the tetracycline class as FDA-approved treatments for plague.

While the oral fluoroquinolones are effective choices for treatment of community-acquired pneumonia (CAP), joint guidelines from the American Thoracic Society (ATS) and Infectious Diseases Society of America (IDSA) published in 2019 recommend amoxicillin, doxycycline, or a macrolide for outpatient treatment of CAP in adult patients without comorbidities or risk of antibiotic resistance. For outpatient treatment of CAP in adult with comorbidities, monotherapy with respiratory fluoroquinolone (strong recommendation) or combination therapy with amoxicillin/clavulanate or a cephalosporin plus a macrolide or doxycycline (conditional recommendation) is recommended.[11]

Symptoms of chronic obstructive pulmonary disease (COPD) exacerbation include increased breathlessness, wheezing, chest tightness, increased cough and sputum, change of color and/or tenacity of sputum, and fever. Increased sputum volume and purulence indicates a bacterial cause, as does prior history of chronic sputum production.[12] According to the 2019 update of the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines, all patients with symptoms of COPD exacerbation should be treated with additional bronchodilators with or without glucocorticosteroids. Antibiotic use for exacerbations remains controversial; however, an antibiotic should be given to patients with the following 3 cardinal symptoms: increased dyspnea, increased sputum volume, increased sputum purulence; or to those patients with increased sputum purulence and 1 other cardinal symptom; or to those patients with increased sputum purulence and 1 other cardinal symptom; or those who require mechanical ventilation. Antibiotic selection should be based on local resistance patterns and isolates.

Urinary tract infections (UTI) occur more commonly in women.[13] Acute cystitis is a symptomatic bladder infection characterized by frequency, urgency, dysuria, and suprapubic pain in a woman with a normal genitourinary tract. The 2010 updated IDSA guidelines for the management of acute uncomplicated cystitis considers the optimal approach to antibiotic selection and resistance patterns and the potential for the selection of drug-resistant organisms and colonization or infection for multi-drug resistant organisms. The empiric antibiotic selection for acute uncomplicated cystitis is nitrofurantoin 100 mg twice daily for 5 days. Empiric antibiotic selection may include trimethoprim/sulfamethoxazole double-strength (160/800 mg) twice daily for 3 days when local uropathogens are less than 20% resistant or if the infecting strain is known to be sensitive. The fluoroquinolones, ofloxacin, ciprofloxacin and levofloxacin, are highly efficacious, but use of fluoroquinolones has been linked to infections with methicillin-resistant *Staphylococcus aureus* and with increasing fluoroquinolone resistance in gram negative bacilli. Fluoroquinolones are considered alternatives for acute cystitis (A-III). Acute pyelonephritis is a renal infection with costovertebral angle

pain and tenderness, often with fever.[14] A urine culture and susceptibility test should be performed when pyelonephritis is suspected. Ciprofloxacin oral with or without an initial parenteral ciprofloxacin 400 mg dose is an appropriate selection for patients not requiring hospitalization. Prevalence of resistant local community uropathogens to fluoroquinolones should not exceed 10%. The first antimicrobial dose given parenterally may include ceftriaxone or an aminoglycoside (24 hour dosing method preferred) rather than a fluoroquinolone, especially when fluoroquinolone-resistant uropathogens are expected to exceed 10%. Alternative oral fluoroquinolone regimens include ciprofloxacin ER for 7 days or levofloxacin 750 mg daily for 5 days.

For the treatment of pelvic inflammatory disease (PID), the 2015 Centers for Disease Control and Prevention (CDC) sexually transmitted diseases guidelines recommend oral antibiotic therapy for patients with mild to moderately severe symptoms.[15] Since PID can be caused by more than 1 organism, PID should be treated with antibiotics effective against a wide range of infectious agents. Oral regimens have been shown to provide outcomes similar to parenteral therapy. Infection with *N. gonorrhoeae* is a major cause of PID, and tests for gonorrhea must be performed prior to initiating therapy. The new CDC guidelines recommend combination therapy with ceftriaxone 250 mg intramuscularly and either azithromycin 1 g orally as a single dose or doxycycline 100 mg orally twice daily for 7 days as the most effective treatment for uncomplicated gonorrhea. Fluoroquinolones are no longer recommended routinely due to resistance, but may be considered if local resistance is low and cephalosporin therapy is not an option for the patient (e.g., allergy). The 2016 World Health Organization (WHO) guideline update also states quinolones are not recommended for the treatment of gonorrhoea due to high levels of resistance.[16] In addition, fluoroquinolones are not effective therapies for syphilis[17]

The current (2014) IDSA Practice Guidelines for the Diagnosis and Management of Skin and Soft-Tissue Infections update include fluoroquinolones as an alternative to amoxicillin-clavulanate in the treatment of infections due to animal or human bites. Fluoroquinolones are also included in combination therapy of skin infections in immunocompromised patients. Ciprofloxacin and levofloxacin are recommended for the treatment of cutaneous anthrax from presumed aerosol exposure[18,19] As a newly approved agent, delafloxacin is not discussed in these guidelines.

Fluoroquinolones have a limited role in the management of acute sinusitis. According to the 2015 American Academy of Otolaryngology guideline update on the treatment of adult sinusitis, adults with mild or moderate acute bacterial rhinosinusitis (ABRS) may be observed with watchful waiting or treated with amoxicillin. Respiratory fluoroquinolones (levofloxacin, moxifloxacin) may be used for penicillin-allergic patients or patients who failed initial treatment.[20] Updated IDSA guidelines for the management of acute and chronic rhinosinusitis were published in March 2012. The IDSA guidelines recommend respiratory fluoroquinolones as alternative agents for patients with a penicillin allergy, hospitalized patients, and those with high risk for antibiotic resistance (e.g., failure of prior therapy).[21]

In 2016, the FDA advised that the serious side effects involving tendons, muscles, joints, nerves and the central nervous system (CNS) outweigh the benefits in patients being treated for sinusitis, bronchitis and uncomplicated UTIs. Fluoroquinolones should be reserved for use in patients who have no other treatment options for acute bacterial sinusitis, (ABS), acute bacterial exacerbation of chronic bronchitis (ABECB), and uncomplicated urinary tract infections (UTI) because the risk of these serious side effects generally outweighs the benefits in these patients.[22]

In 2018, an FDA review found that systemic fluoroquinolones double the risk of aortic dissections which could lead to dangerous bleeding or death. Individuals at increased risk include those with a history of blockages or aneurysms of the aorta or other blood vessels; patients with peripheral atherosclerotic vascular diseases, high blood pressure, certain genetic disorders that involve blood vessel changes such as Marfan syndrome and Ehlers-Danlos syndrome; and the elderly. The FDA now recommends that fluoroquinolones only be prescribed to these patients when no other treatment options are available.[23]

This review will compare and contrast the relative strengths, weaknesses, and distinguishing characteristics of the members of the oral fluoroquinolones. Few clinical trials directly compare the clinical efficacy and adverse effects of the oral fluoroquinolones.

PHARMACOLOGY

Fluoroquinolones are synthetic, broad-spectrum antibacterial agents. The fluorine molecule provides increased potency against gram-negative organisms and broadens the spectrum to include gram-positive organisms; the piperazine moiety confers antipseudomonal activity. These agents are bactericidal. Fluoroquinolones promote cleavage of bacterial DNA in the DNA-enzyme complexes of DNA gyrase (associated with gram-negative activity) and type IV topoisomerase (associated with gram-positive activity), resulting in rapid bacterial death.[24] Mutations of the topoisomerase IV gene combined with gene mutations that alter DNA gyrase lead to high-level fluoroquinolone resistance in *S. pneumoniae.*[25] Fluoroquinolones exhibit a prolonged post-antibiotic effect (PAE); organisms may not resume growth until 2 to 6 hours after quinolone exposure even at undetectable drug levels.[26]

PHARMACOKINETICS[27,28]

Fluoroquinolones exhibit concentration-dependent (versus time-dependent) bactericidal effects with more pronounced bactericidal activity as serum drug concentrations approach 30 times the minimum inhibitory concentration (MIC) or when the area-under-the-inhibitory-curve (AUIC) exceeds 250.[29,30] The exact level of the targeted AUIC varies in the literature.[31] Fluoroquinolones have a post-antibiotic effect of approximately 1 to 2 hours up to 2 to 6 hours.[32,33]

Fluoroquinolones are well absorbed following oral administration, with bioavailability for most agents in excess of 85%. Exceptions are ciprofloxacin, which is 70% to 80% bioavailable, gemifloxacin (Factive), which is 71% bioavailable, and delafloxacin (Baxdela), which is approximately 59% bioavailable.[34,35,36] Serum drug levels achieved with the other fluoroquinolones, (levofloxacin, moxifloxacin, and ofloxacin), after oral administration are comparable to concentrations achieved with intravenous (IV) dosing. This allows for early transition from IV to oral therapy and potential reduction of treatment costs.[37]

Fluoroquinolones are widely distributed throughout the body with tissue concentrations higher than achieved in plasma. The agents penetrate well into stool, bile, prostatic tissue, lung tissue, urine, and kidneys. Because cerebrospinal fluid concentrations are consistently low, the fluoroquinolones are inadequate for first-line treatment of meningitis.[38] Below is a summary of the pharmacokinetic parameters.

Pharmacokinetic Parameters

Drug	Bioavailability (%)	Half-Life (hr)	Metabolites	Excretion (%)
ciprofloxacin (Cipro)[39]	~ 70	4	Four metabolites – less active than parent (15% of parent dose)	Urine: 40-50 Feces: 20-35
ciprofloxacin extended release (Cipro XR)[40]	--	6.3-6.6	Four metabolites – less active than parent (15% of parent dose)	Urine: 35 Feces: 20-35
delafloxacin (Baxdela)[41]	58.8	3.7-8.5	No significant metabolites	Urine: 50-65 Feces: 28-48
gemifloxacin (Factive)[42]	71	7	N-acetyl, E-isomer, and carbamyl glucuronide of gemifloxacin (<10% of oral dose)	Urine: 36 Feces: 61
levofloxacin (Levaquin)[43]	99	6-8	Desmethyl and N-oxide metabolites (little pharmacological activity)	Urine: 87 Feces: <4
moxifloxacin [44]	90	12	Two metabolites - sulfate and glucuronide conjugates	Urine: 34 Feces: 63
ofloxacin[45]	98	9	Desmethyl and N-oxide metabolites (5% of parent)	Urine: 65-80 Feces: 4-8

* Half-live after oral administration

Antimicrobial Activity

The older fluoroquinolones, ciprofloxacin and ofloxacin, have minimal gram-positive activity, but they are the most active against aerobic gram-negative bacilli. Limited microbial susceptibility and acquired resistance limit the usefulness of older agents in the treatment of staphylococcal, streptococcal, and enterococcal infections.[46] Ciprofloxacin remains the most potent of the fluoroquinolones against some strains of *Pseudomonas aeruginosa*.[47]

Newer fluoroquinolones, delafloxacin, gemifloxacin, levofloxacin, and moxifloxacin, have improved gram-positive coverage as compared to older agents. Newer agents have *in vitro* activity against *S. pneumoniae.* Gemifloxacin, levofloxacin, and moxifloxacin provide coverage for penicillin-resistant and multi-drug resistant strains of *S. pneumoniae.* However, levofloxacin- and fluoroquinolone-resistant *S. pneumoniae* isolates have been reported.[48,49] Compared with levofloxacin, moxifloxacin is 4 to 8 times more active against *S. pneumoniae in vitro.* Moxifloxacin also has shown greater *in vitro* activity against *Staphylococcus aureus* and some enterococcal strains.[50]

The Gonococcal Isolate Surveillance Project (GISP) annual report for 2013 showed continued high prevalence of resistance to both penicillin and tetracycline for gonococcal isolates (> 30%).[51] In 2011, the percentage of ciprofloxacin-resistant strains of gonococcal isolates in the United States increased from 9.6% in 2009 to 16.1% in 2013. Multi-drug resistant gonococcal isolates resistant to penicillin, tetracycline, and fluoroquinolones have been identified. The multidrug resistant gonococcal strains show decreased susceptibility to cefixime, and new guidelines were issued. Cephalosporin monotherapy is no longer recommended for the treatment of gonorrhea according to the CDC. Instead, for treatment of uncomplicated gonococcal infections of the cervix, urethra, pharynx, and rectum, CDC recommends combination therapy with a single intramuscular dose of ceftriaxone 250 mg plus a single dose of azithromycin 1 g orally. [52,53]

The CDC issued a Health Advisory regarding *Shigella* strains with elevated MIC that indicate the likely presence of quinolone resistance gene(s) that may lead to reduced susceptibility to fluoroquinolone antibiotics.[54] The CDC recommends that stool cultures and antimicrobial susceptibility testing should be performed in the face of suspected shigellosis and that antibiotic therapy should be reserved for patients for whom it is clinically indicated or when public health officials advise treatment in an outbreak setting. Fluoroquinolones should not be prescribed if the ciprofloxacin MIC is 0.12 µg/mL or higher even if the laboratory report identifies the isolate as susceptible.

Spectrum of Activity[55,56,57,58,59,60,61,62,63,64]

Drug	Gram-positive bacteria	Gram-negative bacteria		Anaerobic bacteria	Atypical pathogens	STD pathogens
		All Gram negative bacteria	*Pseudomonas* species			
ciprofloxacin (Cipro, Cipro XR)[a]	+	++++	++++	0	++	++
delafloxacin (Baxdela)[65]	++	+++	++	nr	nr	nr
gemifloxacin (Factive)	++[c]	+++	++	nr	+++	nr
levofloxacin (Levaquin)	++[c]	+++	+++	+	+++	+++
moxifloxacin [b]	++[c]	+++	++	++	+++	+++
ofloxacin	+	+++	++	0	+++	+++

nr = not reported

[a] Ciprofloxacin does not provide reliable activity against *Chlamydia*

[b] Only moxifloxacin produces reliable anaerobic activity

[c] Includes activity against penicillin-resistant and multi-drug resistant *Streptococcus pneumoniae* in the setting of CAP

CONTRAINDICATIONS/WARNINGS[66,67,68,69,70,71,72,73,74]

Ciprofloxacin and ciprofloxacin ER (Cipro XR) are contraindicated with coadministration of tizanidine (Zanaflex®).

The labeling for all oral fluoroquinolones now includes a boxed warning regarding the increased risk of tendonitis and tendon rupture in all ages. These serious adverse effects involving tendons, muscles, joints, nerves, and the central nervous system (CNS) outweigh the benefits in patients being treated for sinusitis, bronchitis, and uncomplicated UTIs; thus, and these drugs are labeled with a limitation of use in these conditions. The risk is further increased in older patients over 60 years of age, in patients taking corticosteroid drugs, and in patients with kidney, heart, or lung transplants. This adverse effect most frequently involves the Achilles tendon, and rupture of the Achilles tendon may require surgical repair. Tendonitis and tendon rupture in the rotator cuff (the shoulder), the hand, the biceps, the thumb, and other tendon sites have also been reported. Other risk factors include strenuous physical activity, renal failure, and previous tendon disorders such as rheumatoid arthritis. Tendonitis and tendon rupture have also occurred in patients taking fluoroquinolones who do not have the above risk

factors. Tendon rupture can occur during or after completion of therapy; cases occurring up to several months after completion of therapy have been reported and effects have lasted 9 years. Fluoroquinolones should be discontinued if the patient experiences pain, swelling, inflammation or rupture of a tendon. Patients should be advised to rest at the first sign of tendonitis or tendon rupture, and to contact their healthcare provider regarding changing to a non-quinolone antimicrobial drug.

Quinolones may also exacerbate muscle weakness in patients with myasthenia gravis; avoid use in patients with known history of the condition.

Pseudomembranous colitis, or *Clostridium difficile*-associated diarrhea (CDAD), has been reported with nearly all antibacterial agents including the oral fluoroquinolones. Pseudomembranous colitis should be considered in patients who present with diarrhea after use of antibacterials.

Serious hypersensitivity and/or anaphylactic reactions have been reported with fluoroquinolone use. Clinical manifestations may include 1 or more of the following: fever, rash, or severe dermatologic reactions (e.g., toxic epidermal necrolysis, Stevens-Johnson syndrome); vasculitis; arthralgia; myalgia; serum sickness; allergic pneumonitis; interstitial nephritis; acute renal insufficiency or failure; hepatitis; jaundice; acute hepatic necrosis or failure; anemia, including hemolytic and aplastic; thrombocytopenia, including thrombotic thrombocytopenic purpura; leukopenia; agranulocytosis; pancytopenia; and/or other hematologic abnormalities. The drug should be discontinued immediately at the first appearance of a skin rash, jaundice, or any other sign of hypersensitivity and supportive measures instituted.

Reports of central nervous system (CNS) stimulation, convulsions, dizziness, confusion, tremors, hallucinations, depression, toxic psychoses, increased intracranial pressure (including pseudotumor cerebri), and suicidal thoughts or acts have been reported following fluoroquinolone administration and levofloxacin has been associated with completed suicide. All fluoroquinolones should be used with caution in patients with known or suspected CNS disorders that predispose a patient to seizures (epilepsy, severe cerebral arteriosclerosis) or lower the seizure threshold or in the presence of other risk factors that may predispose to seizure or can lower the seizure threshold (certain drug therapy, renal dysfunction). Other mental health side effects include disturbances in attention, disorientation, agitation, nervousness, memory impairment, and delirium.

Rare reports of sensory or sensorimotor axonal polyneuropathy affecting small and/or large axons resulting in paresthesias, hypoesthesias, dysesthesias, and weakness have been reported in patients receiving fluoroquinolones. Fluoroquinolones should be discontinued if the patient experiences symptoms of neuropathy including pain, burning, tingling, numbness, weakness, or is found to have deficits in light touch, pain, temperature, position sense, vibratory sensation, or motor strength in order to prevent the development of an irreversible condition.

Fluoroquinolones are not effective therapies for syphilis and are no longer recommended for gonorrhea.[75,76]

Coadministration of ciprofloxacin and theophylline has resulted in serious and fatal reactions. Reactions have included cardiac arrest, seizure, status epilepticus, and respiratory failure. Although similar serious adverse effects have been reported in patients receiving theophylline alone, the possibility that these reactions may be potentiated by ciprofloxacin cannot be eliminated. If concomitant use cannot be avoided, serum levels of theophylline should be monitored and dosage adjustments made as appropriate.

Post-marketing reports of severe and sometimes fatal hepatotoxicity have occurred with levofloxacin (Levaquin) use. Use of levofloxacin should be discontinued immediately if the patient develops signs and symptoms of hepatitis. Severe hepatotoxicity generally occurred within 14 days of initiation of therapy, and most cases occurred within 6 days. Most cases of severe hepatotoxicity were reported in patients over 65 years of age and were not associated with hypersensitivity. Levofloxacin should be discontinued immediately if the patient develops signs and symptoms of hepatitis. Moxifloxacin should be used with caution in patients with mild, moderate, or severe liver cirrhosis.

Moderate to severe photosensitivity or phototoxicity reactions, manifested as exaggerated sunburn reactions involving areas exposed to light, have been associated with the use of fluoroquinolones after sun or UV light exposure. Therefore, excessive exposure to these sources of light should be avoided, and drug therapy should be discontinued if photosensitivity/phototoxicity occurs.

Disturbances of blood glucose, including symptomatic hyper- and hypoglycemia which may lead to coma, have been reported with all fluoroquinolones, usually in elderly diabetic patients receiving concomitant treatment with an oral hypoglycemic agent (e.g. glyburide) or with insulin.[77,78,79] In these patients, careful monitoring of blood glucose is recommended. If a hypoglycemic reaction occurs in a patient being treated with levofloxacin or ofloxacin, therapy should be discontinued and appropriate therapy should be initiated immediately. The concomitant administration of ciprofloxacin with glyburide has, on rare occasions, resulted in severe hypoglycemia. No clinically significant changes in blood glucose were reported with moxifloxacin when given with glyburide.

QTc interval prolongation

As a class, fluoroquinolones have been associated with QTc interval prolongation. Fluoroquinolones have warnings in the product labeling to avoid use of these drugs in patients with pre-existing prolonged QTc interval, in those receiving agents concurrently known to prolong the QTc interval, in patients with uncorrected hypokalemia, or those receiving Class IA or III antiarrhythmics.[80,81,82,83,84,85] QTc interval prolongation appears to be a dose-related effect; recommended dosages should not be exceeded. Reduce the dosage of all fluoroquinolones except moxifloxacin for patients with renal insufficiency to avoid excessively high serum levels. No excess in cardiovascular morbidity or mortality has been reported in over 15,500 patients in controlled studies, and there was no increased mortality in 18,000 patients receiving oral moxifloxacin in post-marketing trials where ECGs were not monitored.[86]

Fluoroquinolones prolong the QT interval by blocking voltage-gated potassium channels, especially the rapid component of the delayed rectifier potassium current I(Kr), expressed by hERG (the human ether-a-go-go-related gene). According to the available case reports and clinical studies, moxifloxacin carries the greatest risk of QT prolongation from all available quinolones in clinical practice and it should be used with caution in patients with predisposing factors for Torsades de Pointes (TdP). Although gemifloxacin, levofloxacin, and ofloxacin are associated with a lower risk of QT prolongation compared with moxifloxacin, they should also be used with caution in patients at risk for QT prolongation. Ciprofloxacin appears to be associated with the lowest risk for QT prolongation and the lowest TdP rate.[87]

In the double-blind CAPRIE trial, moxifloxacin IV/oral and levofloxacin IV/oral were compared for cardiac rhythm safety in 394 elderly hospitalized patients for the treatment of community acquired pneumonia (CAP).[88] Holter monitoring for at least 3 days revealed a ventricular arrhythmia rate of 8.3%

and 5.1% for moxifloxacin and levofloxacin; this difference was not statistically significant. Nonsustained ventricular tachycardia occurred in 7.3% of patients receiving moxifloxacin and 5.1% of patients receiving levofloxacin. One case of sustained monomorphic ventricular tachycardia occurred in the moxifloxacin group. One patient on levofloxacin developed torsades de pointes.

QTc Warnings

Drug	Cases of TdP per 10 million Rx (95% CI)[89]	QT guidance	Guidance for patients at high risk
ciprofloxacin (Cipro)[90,91]	0.3 (0-1.1)	In general, elderly patients may be more susceptible to drug associated effects on the QT interval.	Caution should be taken when using ciprofloxacin with concomitant drugs that can cause QT interval prolongation (i.e. class IA or class III antiarrhythmics) or patients with risk factors for torsades de pointes (i.e. known QT prolongation, uncorrected hyperkalemia).
delafloxacin (Baxdela)[92]	no data	Delafloxacin did not prolong QT at concentrations 3.4 fold higher than achieved with oral dosing	--
gemifloxacin (Factive)[93]	no data	Fluoroquinolones may prolong the QT interval in some patients.	Gemifloxacin should be avoided in patients with a history of prolongation of the QTc interval, patients with uncorrected electrolyte disorders (hypokalemia or hypomagnesemia), and patients receiving Class IA (e.g. quinidine, procainamide) or Class III (e.g. amiodarone, sotalol) antiarrhythmic agents. Pharmacokinetic interaction studies between gemifloxacin and drugs that prolong the QTc interval such as erythromycin, antipsychotics, and tricyclic antidepressants have not been performed. Gemifloxacin should be used with caution when given concurrently with these drugs, as well as in patients with ongoing proarrhythmic conditions, such as clinically significant bradycardia or acute myocardial ischemia. The likelihood of QTc prolongation may increase with increasing dose of the drug; therefore, the recommended dose should not be exceeded especially in patients with renal or hepatic impairment where the Cmax and AUC are slightly higher. QTc prolongation may lead to an increased risk for ventricular arrhythmias including torsades de pointes. The maximal change in the QTc interval occurs approximately 5-10 hours following oral administration of gemifloxacin.

QTc Warnings (continued)

Drug	Cases of TdP per 10 million Rx (95% CI)[94]	QT guidance	Guidance for patients at high risk
levofloxacin (Levaquin)[95]	5.4 (2.9-9.3)	Some quinolones, including levofloxacin, have been associated with prolongation of the QT interval on the ECG and infrequent cases of arrhythmia.	Rare cases of torsades de pointes have been spontaneously reported during postmarketing surveillance in patients receiving quinolones, including levofloxacin. Levofloxacin should be avoided in patients with known prolongation of QT interval, patients with uncorrected hypokalemia, and patients receiving class IA (quinidine, procainamide) and class III (sotalol, amiodarone) antiarrhythmic agents. Elderly patients may be more susceptible to drug-associated effects on the QT interval.
moxifloxacin [96]	0 (0-26)	Moxifloxacin has been shown to prolong the QT interval of the ECG in some patients.	Moxifloxacin should be avoided in patients with known prolongation of the QT interval, patients with uncorrected hypokalemia and patients receiving Class IA or Class III antiarrhythmic agents, due to the lack of clinical experience with the drug in these patient populations. Pharmacokinetic interaction studies between moxifloxacin and other drugs that prolong the QT interval such as cisapride, erythromycin, antipsychotics, and tricyclic antidepressants have not been performed. An additive effect of moxifloxacin and these drugs cannot be excluded; therefore, moxifloxacin should be used with caution when given concurrently with these drugs.
ofloxacin[97]	2.1 (0.3-7.6)	Some quinolones, including ofloxacin, have been associated with prolongation of the QT interval on the ECG and infrequent cases of arrhythmia.	Rare cases of torsades de pointes have been spontaneously reported during post-marketing surveillance in patients receiving quinolones, including ofloxacin. Ofloxacin should be avoided in patients with known prolongation of the QT interval, patients with uncorrected hypokalemia, and patients receiving Class IA (quinidine, procainamide), or Class III (amiodarone, sotalol) antiarrhythmic agents.

DRUG INTERACTIONS

Drug	theophylline	phenytoin	cyclosporine	warfarin	digoxin	Class IA and III antiarrhythmics
ciprofloxacin (Cipro, Cipro XR)[98,99]	X	X	X	X	-	X
delafloxacin (Baxdela)[100]	not studied	not studied	not studied	not studied	not studied	not studied
gemifloxacin (Factive)[101]	-	not studied	not studied	-	-	X
levofloxacin (Levaquin)[102]	consider monitoring	-	-	reported	-	X
moxifloxacin [103]	-	-	-	X	-	X
ofloxacin[104]	X	-	-	-	-	X

Oral fluoroquinolones should not be administered at the same time as antacids, multi-valent cation drugs including sucralfate, chewable/buffered didanosine, metal cations such as iron and calcium, and multivitamins containing zinc due to reduced bioavailability of the fluoroquinolone. For ofloxacin and

levofloxacin, administer the fluoroquinolone at least 2 hours before and 2 hours after the administration of antacids and multi-valent cation drugs. For gemifloxacin, the time frame is a minimum of 3 hours before and 2 hours after for all metal cations except calcium carbonate. Administer gemifloxacin at least 2 hours before and 2 hours after calcium carbonate and sucralfate. For ciprofloxacin and delafloxacin administer the fluoroquinolone at least 2 hours before and at least 6 hours after the metal cation drugs. For moxifloxacin, administration should be at least 4 hours before and at least 8 hours after.

Disturbances of blood glucose, including hyperglycemia and hypoglycemia, have been reported in patients treated concomitantly with some fluoroquinolones and an antidiabetic agent.[105] Therefore, careful monitoring of blood glucose is recommended when levofloxacin and ofloxacin are coadministered with an antidiabetic agent.

ADVERSE EFFECTS

Drug	Nausea	Diarrhea	Dizziness	Vomiting	Abdominal pain	Headache	Phototoxicity
ciprofloxacin (Cipro)[106] n=49,038	2.5	1.6	< 1	1	< 1	<1	< 1
ciprofloxacin ER (Cipro XR)[107] n=961	4	2	2	2	< 1	3	< 1
delafloxacin (Baxdela)[108] n=741	8	8	< 2	2	reported	3	nr
gemifloxacin (Factive)[109] n=8,119	3.7	5	1.7	1.6	2.2	4.2	≤ 0.1
levofloxacin (Levaquin)[110] n=7,537	7	5	3	2	2	6	reported
moxifloxacin[111] n= >15,500	6	5	2	0.1-2	0.1-2	0.1-2	< 0.1
ofloxacin[112]	10	4	5	4	1-3	9	reported

Adverse effects are reported as a percentage. Adverse effects data are obtained from package inserts and are not meant to be comparative or all inclusive. nr = not reported.

Photosensitivity/phototoxicity warnings appear in the prescribing information for all oral fluoroquinolones. Patients taking a fluoroquinolone are advised to avoid excessive exposure to sunlight or artificial ultraviolet light to prevent skin eruptions or sunburns.

Rash, most commonly described as maculopapular and mild to moderate in severity, has been reported in 0.4% to 4% of patients receiving gemifloxacin (Factive) with the highest occurrence seen in women less than 40 years old taking gemifloxacin for 7 days (12% of women less than 40 years old) or 10 days (15.3% of women less than 40 years old).[113] Women taking hormone replacement therapy and gemifloxacin were also observed to have a higher rate of rash than men. Gemifloxacin therapy is not recommended to exceed 7 days. Longer duration of treatment is associated with a higher incidence of

rash in all patients except men over 40 years of age. Gemifloxacin should be discontinued when a rash appears. Eighty percent of rashes resolved within 14 days. Approximately 10% of the rashes (0.5% of all patients) were described as of severe intensity and approximately 10% of those with rash were treated with systemic steroids.

SPECIAL POPULATIONS[114,115,116,117,118,119,120]

Pediatrics

In initial studies of fluoroquinolones, bone and joint abnormalities (osteochondrosis) were seen in young dogs. Permanent damage to cartilage in weight-bearing joints was concerning. Adverse effects in tendons have been reported. Benefits of systemic fluoroquinolone use versus risks associated with use in pediatrics must be considered. [121] The American Academy of Pediatrics and Pediatric Infectious Diseases Society/Infectious Diseases Society of America guidelines on community-acquired pneumonia in children support the use of levofloxacin as an alternative therapy for those with severe penicillin allergy and for those infected with suspected multidrug-resistant pneumococcus (i.e., patients in whom amoxicillin and amoxicillin-clavulanate have failed. Otitis media and acute bacterial sinusitis guidelines from the American Academy of Pediatrics state that fluoroquinolone use in children should only be considered when there are no other safe or effective alternatives to treatment of an infection caused by multi-drug resistant bacteria or to provide oral therapy when parenteral treatment is not feasible, and no other oral agent is effective. Since 2006, the clinical value of fluoroquinolones in children with particular infections (especially gram-negative infections) has been documented. Some quinolones are currently approved by the FDA for urinary tract infections (nalidixic acid), inhalational anthrax (ciprofloxacin and levofloxacin), plague (ciprofloxacin and levofloxacin), pyelonephritis and complicated UTI (ciprofloxacin).[122] Safety and effectiveness of gemifloxacin (Factive), moxifloxacin , delafloxacin (Baxdela), and ofloxacin have not been established in children less than 18 years of age.

Ciprofloxacin is indicated for patients younger than 18 years of age for the treatment of complicated urinary tract infections and for pyelonephritis in children ages 1 to 17 years.[123] Ciprofloxacin is not a first choice antimicrobial in pediatrics due to increased adverse events compared to controls including events related to joints and/or surrounding tissues over 6 weeks (9.3% ciprofloxacin-treated patients versus 6% in control-treated patients). Ciprofloxacin and levofloxacin (Levaquin) are indicated in the treatment of inhalational anthrax (post-exposure) for children greater than 6 months of age. Levofloxacin also has an indication for use in pediatric patients aged 6 months and older for both treatment and prophylaxis of plague. An increased incidence of musculoskeletal disorders such as arthralgia, arthritis, tendinopathy, and gait abnormality have been reported in pediatric patients receiving ciprofloxacin or levofloxacin compared to controls. Ciprofloxacin ER (Cipro XR) has not been studied in children.[124]

Pregnancy

Fluoroquinolones are all Pregnancy Category C with the exception of delafloxacin, which has not been assigned a pregnancy category in compliance with the Pregnancy and Lactation Labeling Rule (PLLR). Data on the use of delafloxacin in pregnant women are insufficient to inform of a drug-related risk of birth defects or miscarriage.

Geriatrics

Geriatric patients are at increased risk for developing severe tendon disorders including tendon rupture when being treated with a fluoroquinolone. Concomitant systemic corticosteroids further increase the risk. Tendon disorders may involve the Achilles, hand, shoulder, or other tendon sites and can occur during or after completion of therapy; cases occurring up to several months after fluoroquinolone treatment have been reported.

Renal Insufficiency

All fluoroquinolones, except moxifloxacin, require adjustment of dose and/or interval for patients with renal insufficiency. For delafloxacin (Baxdela) dosage adjustments are only necessary with the oral formulation in patients with end-stage renal disease (ESRD) on dialysis.

Hepatic Insufficiency

No dosage adjustment is recommended for mild, moderate, or severe hepatic insufficiency (Child Pugh Classes A, B or C) for moxifloxacin. However, due to metabolic disturbances associated with hepatic insufficiency, which may lead to QT prolongation, moxifloxacin should be used with caution in this patient population. The excretion of ofloxacin may be reduced in patients with severe liver function disorders (e.g. cirrhosis with or without ascites). A maximum dose of 400 mg of ofloxacin per day should therefore not be exceeded. No dosage adjustment of delafloxacin is required in patients with hepatic impairment.

SELECTED DOSAGES[125,126,127,128,129,130,131]

Drug and Availability	AECB/Lower respiratory tract infection	CAP	Acute Sinusitis	Plague	Prostatitis	Skin	UTI (regimen selected based on the severity of infection)
ciprofloxacin (Cipro) 100 mg, 250 mg, 500 mg, 750 mg tablets; 250 mg/5 mL (5%) and 500 mg/5 mL (10%) suspension	500-750 mg every 12 hours for 7-14 days	--	500 mg every 12 hours for 10 days	--	500 mg every 12 hours for 28 days	500-750 mg every 12 hours for 7-14 days	250 mg every 12 hours for 3 days; 250-500 mg every 12 hours for 7-14 days Pediatrics: 10-20 mg/kg every 12 hours (not to exceed 750 mg) for 10-21 days
ciprofloxacin ER (Cipro XR) 500 mg, 1,000 mg tablets	--	--	--	--	--	--	500 mg daily for 3 days; 1,000 mg daily for 7-14 days
delafloxacin (Baxdela) 450 mg tablets	--	450 mg every 12 hours for 5 to 10 days	--	--	--	450 mg every 12 hours for 5 to 14 days	--
gemifloxacin (Factive) 320 mg tablets	320 mg daily for 5 days	320 mg daily for 5-7 days	--	--	--	--	--

Selected Dosages (continued)

Drug and Availability	AECB/Lower respiratory tract infection	CAP	Acute Sinusitis	Plague	Prostatitis	Skin/Skin-Structure	UTI (regimen selected based on the severity of infection)
levofloxacin (Levaquin)* 250 mg, 500 mg, 750 mg tablets; 25 mg/mL oral solution	500 mg daily for 7 days	500 mg daily for 7-14 days 750 mg daily for 5 days	500 mg daily for 10-14 days 750 mg daily for 5 days	500 mg daily for 10-14 days	500 mg daily for 28 days	500-750 mg every 12 hours for 7-14 days	250 mg daily for 3-10 days or 750 mg daily for 5 days
moxifloxacin 400 mg tablets	400 mg daily for 5 days	400 mg daily for 7-14 days	400 mg daily for 10 days	--	--	400 mg daily for 7-21 days	--
ofloxacin 300 mg, 400 mg tablets	400 mg every 12 hours for 10 days	400 mg every 12 hours for 10 days	--	--	300 mg every 12 hours for 6 weeks	400 mg every 12 hours for 10 days	200 mg every 12 hours for 3-10 days

* Dosing regimens for levofloxacin vary based on suspected or confirmed organism and/or regimen selected.

All fluoroquinolones except moxifloxacin require dosage adjustment in patients with renal impairment.

Ciprofloxacin ER (Cipro XR) tablets should not be crushed, chewed or split.

Gemifloxacin (Factive) tablets should be swallowed whole with plenty of liquid and may be taken without regard to food.

Levofloxacin (Levaquin) solution should be given 1 hour before or 2 hours after a meal. Levofloxacin tablets may be given without regard to food.

Delafloxacin (Baxdela) dosage is 450 mg every 12 hours for 5 to 14 days for skin and soft tissue infections

CLINICAL TRIALS

Search Strategies

Studies were identified through searches performed on PubMed and review of information sent by manufacturers. Search strategy included the FDA-approved use of all drugs in this class. Randomized, controlled trials performed in the United States comparing oral agents within this class within the last 7 years in an outpatient setting for the approved indications are considered the most relevant in this category. Studies included for analysis in the review were published in English, performed with human participants and randomly allocated participants to comparison groups. In addition, studies must contain clearly stated, predetermined outcome measure(s) of known or probable clinical importance, use data analysis techniques consistent with the study question, and include follow-up (endpoint assessment) of at least 80% of participants entering the investigation. Despite some inherent bias found in all studies including those sponsored and/or funded by pharmaceutical manufacturers, the studies in this therapeutic class review were determined to have results or conclusions that do not suggest systematic error in their experimental study design. While the potential influence of manufacturer sponsorship/funding must be considered, the studies in this review have also been evaluated for validity and importance.

Numerous clinical trials were published comparing the fluoroquinolones in both inpatient and outpatient settings in the 1990s. Little evidence exists that shows 1 fluoroquinolone is superior to others for the approved indications when given in equivalent dosages. Due to changes in susceptibility of *Pseudomonas* and other organisms to fluoroquinolones since the 1990s, only studies published since 2000 are included.[132] Nationwide and regional variances in pathogen susceptibility and resistance rates must be taken into consideration when evaluating studies. Many short-term clinical trials in outpatients with minor infections lose a significant portion of patients due to lack of follow-up. Losses are greater than 25% of enrolled patients in some trials.

Many trials performed with the fluoroquinolones compare the agents to other broad-spectrum antibiotics such as macrolides, cephalosporins, and extended-spectrum penicillins. While relative efficacy is important, the comparisons lend little insight into relative efficacy and safety of agents within this class. Studies comparing available fluoroquinolones to trovafloxacin (Trovan), gatifloxacin (Tequin), and lomefloxacin (Maxaquin) were not included as these fluoroquinolones are no longer available in the United States. Studies of delafloxacin (Baxdela) compared it to an intravenous regimen of vancomycin plus aztreonam for noninferiority; noninferiority was demonstrated.[133,134,135]

Efficacy studies of levofloxacin for plague could not be conducted in humans with plague for ethical and feasibility reasons. Therefore, approval of this indication was based on an efficacy study conducted in animals.[136]

The literature review is current through March 2, 2020.

ciprofloxacin ER (Cipro XR) and ciprofloxacin (Cipro)

In a multicenter, randomized, double-blind, double-dummy Phase III trial consisting of 891 women with acute uncomplicated UTI, pyuria, and a positive pre-therapy urine culture ($\geq 10^5$ colony-forming units/mL), ciprofloxacin ER 500 mg daily for 3 days was compared to ciprofloxacin 250 mg twice daily for 3 days for bacterial eradication.[137] Clinical response rates were 95.5% and 92.7% for ciprofloxacin

ER and ciprofloxacin, respectively (95% CI, -1.6 to 7.1). Bacterial eradication rates were 94.5% and 93.7% for ciprofloxacin ER and ciprofloxacin, respectively (95% CI, -3.5 to 5.1). The most common pathogens were *E. coli, Enterococcus faecalis, Proteus mirabilis*, and *Staphylococcus saprophyticus*.

Ciprofloxacin ER 1,000 mg once daily and ciprofloxacin 500 mg twice daily were compared in 1,035 patients with complicated urinary tract infections or acute uncomplicated pyelonephritis.[138] Treatment continued for 7 to 14 days. In the randomized, double-blind, North American trial, patients were enrolled if they had a positive pre-treatment urine culture and pyuria in the preceding 48 hours. Bacteriologic efficacy determined between 5 and 11 days after treatment initiation were 89% and 85% for ciprofloxacin ER and ciprofloxacin, respectively (95% CI, -2.4 to 10.3). Clinical cure rates were similar with 97% for ciprofloxacin ER and 94% for ciprofloxacin (95% CI, -1.2 to 6.9). Late follow-up was done 28 to 42 days after therapy initiation; similar cure rates were observed. *E. coli* was the most common organism identified in urine cultures. Similar rates of adverse events were reported.

The efficacy and safety of ciprofloxacin ER and ciprofloxacin were compared in 523 adult women with acute uncomplicated UTI.[139] In a multicenter, randomized, double-blind study, patients with a positive pre-treatment urine culture were randomized to ciprofloxacin ER 500 mg once daily or ciprofloxacin 250 mg twice daily. Treatment duration was 3 days. At the test of cure visit (days 4 to 11 after therapy), microbiological eradication rates were 93.4% and 89.6% for ciprofloxacin ER and ciprofloxacin, respectively. Clinical cure rates were 85.7 for ciprofloxacin ER and 86.1% for ciprofloxacin. After 4 to 6 weeks, microbiological and clinical outcomes were similar between the groups. Nausea (0.6% versus 2.2%) and diarrhea (0.2% versus 1.4%) were lower in the ciprofloxacin ER group.

gemifloxacin (Factive) and levofloxacin (Levaquin)

In a randomized, double-blind, double dummy, multicenter, parallel-group study, a total of 360 adults with acute exacerbation of chronic bronchitis (AECB) were randomly assigned to receive gemifloxacin 320 mg daily for 5 days or levofloxacin 500 mg daily for 7 days.[140] A total of 335 patients completed the study. In the intent-to-treat population, clinical success rate at follow-up was 85.2% for gemifloxacin and 78.1% for levofloxacin. The clinical efficacy of gemifloxacin for 5 days in AECB was at least as good as levofloxacin for 7 days. Fewer patients withdrew from the gemifloxacin arm of the trial. (p=0.02).

Five-day fluoroquinolone therapy is associated with faster recovery, fewer relapses, and less hospitalization. Both moxifloxacin and gemifloxacin are FDA approved for 5-day therapy in AECB.[141]

levofloxacin (Levaquin) and ciprofloxacin (Cipro)

In a multicenter, randomized, double-blind trial, levofloxacin 500 mg daily and ciprofloxacin 500 mg twice daily were compared for efficacy and safety in the treatment of chronic bacterial prostatitis in 377 patients.[142] Treatment duration was 28 days. Clinical success rates, which included both cured and improved patients, were similar between the 2 drugs (levofloxacin 75%; ciprofloxacin 72.8%). Bacteriological eradication rates were similar with 75% and 76.8% for levofloxacin and ciprofloxacin, respectively. The most common pathogens were *E. faecalis* and *E. coli*. Six-month relapse rates were also similar. Both drugs were well tolerated.

Fluoroquinolones are the agent of choice for treating bacterial caused prostatitis and in some cases of chronic prostatitis when a causal organism has not been identified.[143] In European men (n=117) a study was done using levofloxacin 500 mg/day in those diagnosed with chronic bacterial prostatitis. In this group there was a 92% success rate (95% CI 84.8% - 96.5%) at 5 to 12 days post treatment.

A multicenter, double-blind trial compared the efficacy and safety of levofloxacin 750 mg intravenously (IV) or orally daily for 5 days to ciprofloxacin 400 mg IV and/or 500 mg orally twice daily for 10 days for the treatment of complicated UTIs or acute pyelonephritis.[144] Patients were evaluated at the end of therapy, post-therapy and post-study for microbiologic eradication and clinical outcomes. A total of 1,109 subjects were enrolled; 619 with confirmed diagnosis of acute pyelonephritis or UTI and a uropathogen with a colony count 10^5 colony forming units/mL or greater were included in the modified intent-to-treat population. The eradication rates in the modified intent-to-treat population at the end of therapy were 79.8% for levofloxacin- and 77.5% for ciprofloxacin-treated patients (95% CI, -8.8 to 4.1). In the microbiologically evaluable population (n=506), eradication rates were 88.3% for levofloxacin and 86.7% for ciprofloxacin-treated subjects (95% CI, -7.4% to 4.2%). Outcomes were comparable for the 2 treatments at the post-therapy and post-study visits. The manufacturer of levofloxacin supported the study.

SUMMARY

Oral fluoroquinolones vary in the spectrum of antimicrobial activity. The older fluoroquinolones have a gram-negative spectrum of activity and are useful in the treatment of urological infections. Newer fluoroquinolones have broad spectrums of activity covering both gram-negative and gram-positive bacteria, and some agents are useful in the treatment of penicillin-resistant *S. pneumoniae*. Delafloxacin (Baxdela), the newest fluoroquinolone with a spectrum including with methicillin-resistant *Staphylococcus aureus* (MRSA), is indicated for the treatment of skin and skin structure infections, as well as for the treatment of CAP.

Fluoroquinolones effectively treat urinary tract infections and CAP, although fluoroquinolones are not considered first-line empiric antibiotics for these infections. In the treatment of CAP in healthy patients, empiric antibiotics include amoxicillin, azithromycin, or clarithromycin or doxycycline. Gemifloxacin (Factive), levofloxacin (Levaquin), and moxifloxacin, the respiratory fluoroquinolones, are active against multi-drug resistant *S. pneumoniae* and should be considered in the presence of comorbidities such as chronic heart, lung, liver, or renal disease; diabetes mellitus; alcoholism; malignancy; or asplenia Levofloxacin is an option for use in the treatment and prevention of plague in both pediatrics and adults.

For the treatment of UTIs, empiric antibiotics may include 1 of the following: trimethoprim/sulfamethoxazole, amoxicillin, nitrofurantoin, or a cephalosporin. Ciprofloxacin and ciprofloxacin ER (Cipro XR), levofloxacin (Levaquin), and ofloxacin are indicated for the treatment of uncomplicated UTIs when there are no other treatment options. Likewise, due to adverse effects, the FDA has recommended that fluoroquinolones be reserved for when there are no other treatment options for a handful of indications and patient populations.

Many factors must be considered when choosing the most appropriate fluoroquinolone for a particular patient. Culture and sensitivity information should guide antibiotic selection when available. Little evidence exists suggesting clinical outcomes, safety, and tolerability differ among the fluoroquinolones when administered for appropriate indications.

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