Therapeutic Class Overview
Fluoroquinolones

INTRODUCTION

- The fluoroquinolones are broad-spectrum antibiotics grouped into generations based on their spectrum of activity (Bolon, 2011).
  - First generation agents, which are structurally quinolones rather than fluoroquinolones, possess activity against aerobic gram-negative bacteria but are not effective against aerobic gram-positive bacteria or anaerobes.
    - The first generation agents (eg, nalidixic acid, cinoxacin) are no longer on the market.
  - Second generation agents, the original fluoroquinolones, contain a fluorine atom at position C-6. These agents offer improved coverage against gram-negative bacteria and moderately improved gram-positive coverage.
    - The available second generation fluoroquinolones include ciprofloxacin, levofloxacin, and ofloxacin. Lomefloxacin and norfloxacin are second generation agents which are no longer on the market.
  - Third generation agents achieve greater potency against gram-positive bacteria, particularly pneumococci, and also possess good activity against anaerobes.
    - All three of the third generation agents, gatifloxacin, grepafloxacin, and sparfloxacin, were removed from the market due to toxicities.
  - Fourth generation fluoroquinolones have superior coverage against pneumococci and anaerobes. These agents include moxifloxacin and gemifloxacin. One additional agent, trovafloxacin, was removed from the market due to toxicities.
  - The most recently approved fluoroquinolone, delafloxacin, has an even broader spectrum of antibiotic activity and is commonly referred to as a “next generation” fluoroquinolone.
- The fluoroquinolones have been used to treat a variety of infections including urinary tract infections, sinusitis, lower respiratory tract infections, intra-abdominal infections, infectious diarrhea, skin and skin structure infections, sexually transmitted diseases, and bacterial prostatitis. A few of the agents also have Food and Drug Administration (FDA) approval for inhalational anthrax and plague. There is also considerable off-label data for use in neutropenic patients and for treatment of tuberculosis and mycobacteria infections in patients with human immunodeficiency virus (HIV). Due to the boxed warning for disabling and potentially irreversible serious adverse reactions involving the tendons, muscles, joints, nerves, and central nervous system, fluoroquinolones should be reserved for patients with no other treatment options when used to treat acute sinusitis, acute bronchitis, and uncomplicated urinary tract infections (FDA press release, 2016).
- As with all antibiotics, local resistance patterns should be considered when prescribing these agents.
- Ciprofloxacin, delafloxacin, levofloxacin, and moxifloxacin are available as intravenous and oral formulations. Ciprofloxacin, levofloxacin, moxifloxacin, and ofloxacin are available in otic and/or ophthalmic formulations. Only the oral formulations and indications will be included in this review.
- Medispan class: Fluoroquinolones

Table 1. Medications Included Within Class Review

Drug	Generic Availability
Avelox (moxifloxacin)	✔
Baxdela (delafloxacin)	-
Cipro (ciprofloxacin)	✔
ciprofloxacin extended release*	✔
Factive (gemifloxacin)	-
Levaquin (levofloxacin)	✔
ofloxacin†	✔

* The branded product, Cipro XR, is no longer marketed.
† The branded product, Floxin, is no longer marketed.
(Drugs@FDA, 2017; Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations, 2017)

INDICATIONS

Table 2. Food and Drug Administration Approved Indications

Indication	Avelox (moxifloxacin)	BAXDELA (delafloxacin)	Cipro (ciprofloxacin)	ciprofloxacin extended release	Factive (gemifloxacin)	Levaquin (levofloxacin)	ofloxacin
Acute bacterial sinusitis caused by *Streptococcus pneumoniae*, *Haemophilus influenzae*, or *Moraxella catarrhalis*.	✔ ∞		✔ ∞			✔ ∞	
Acute bacterial exacerbation of chronic bronchitis caused by *S. pneumoniae* or *H. influenzae.*							✔ ∞
Acute bacterial exacerbation of chronic bronchitis caused by *S. pneumoniae*, *H. influenzae*, *Haemophilus parainfluenzae, Klebsiella pneumoniae,* methicillin-susceptible *Staphylococcus aureus, or M. catarrhalis.*	✔ ∞				✔ ‡ ∞	✔ ǂ ∞	
Community acquired pneumonia caused by *S. pneumoniae* or *H. influenzae.*							✔
Community acquired pneumonia caused by *S. pneumoniae**, *H. influenzae*, *M. catarrhalis,* methicillin-susceptible *S. aureus, K. pneumoniae, Mycoplasma pneumoniae, or Chlamydia pneumoniae.*	✔				✔ ǂǂ	✔ ∫	
Lower respiratory tract infections caused *by Escherichia coli, K. pneumoniae, Enterobacter cloacae, Proteus mirabilis, Pseudomonas aeruginosa, H. influenzae, H. parainfluenzae*, or penicillin-susceptible *S. pneumoniae*.** Also, *M. catarrhalis* for the treatment of acute exacerbations of chronic bronchitis.			✔				
Uncomplicated skin and skin structure infections caused by methicillin-susceptible *S. aureus* or *Streptococcus pyogenes.*	✔					✔	
Uncomplicated skin and skin structure infections caused by methicillin-susceptible *S. aureus*, *S. pyogenes,* or *P. mirabilis.*							✔
Complicated skin and skin structure infections caused by methicillin-susceptible *S. aureus, E. coli, K. pneumoniae, or E. cloacae.*	✔						
Complicated skin and skin structure infections caused by methicillin-susceptible *S. aureus, S. pyogenes, Enterococcus faecalis,* or *P. mirabilis.*						✔	
Skin and skin structure infections caused by *E. coli*, *K. pneumoniae*, *E. cloacae*, *P. aeruginosa*, methicillin-resistant and methicillin-susceptible *S. aureus*, *S. haemolyticus*, *S. lugdunensis*, *S. agalactiae*, *S. anginosus* Group, *S. pyogenes*, and *E. faecalis*		✔					
Skin and skin structure infections caused by *E. coli, K. pneumoniae, E. cloacae, P. mirabilis, Proteus vulgaris, Providencia stuartii, Morganella morganii, Citrobacter freundii, P. aeruginosa*, methicillin-susceptible *S. aureus*, methicillin-susceptible *Staphylococcus epidermidis,* or *S. pyogenes.*			✔				
Bone and joint infections caused by *E. cloacae, Serratia marcescens*, or *P. aeruginosa*.			✔				
Complicated intra-abdominal infections caused by *E. coli, Bacteroides fragilis, Streptococcus anginosus, Streptococcus constellatus, E. faecalis, P. mirabilis, Clostridium perfringens, Bacteroides thetaiotaomicron,* or	✔						

Indication	Avelox (moxifloxacin)	BAXDELA (delafloxacin)	Cipro (ciprofloxacin)	ciprofloxacin extended release	Factive (gemifloxacin)	Levaquin (levofloxacin)	ofloxacin
Peptostreptococcus species.							
Complicated intra-abdominal infections (used in combination with metronidazole) caused by *E. coli, P. aeruginosa, P. mirabilis, K. pneumoniae*, or *B. fragilis*.			✔				
Uncomplicated urinary tract infection (acute cystitis) caused by *E. coli, P. mirabilis, E. faecalis,* or *Staphylococcus saprophyticus.*				✔ ∞			
Uncomplicated urinary tract infection caused by *E. coli, K. pneumoniae,* or *S. saprophyticus.*						✔ ∞	
Complicated urinary tract infection caused by *E. coli, P. mirabilis, K. pneumoniae, E. faecalis,* or *P. aeruginosa.*				✔		✔ ǂǂ	
Complicated urinary tract infection caused by *E. coli, P. mirabilis, K. pneumoniae, P. aeruginosa, or Citrobacter diversus.*							✔
Acute uncomplicated pyelonephritis caused by *E. coli.*				✔		✔	
Urinary tract infection caused by *E. coli, K. pneumoniae, E. cloacae, Serratia marcescens, P. mirabilis, Providencia rettgeri, Morganella morganii, Citrobacter koseri* (*diversus*), *Citrobacter freundii, P. aeruginosa,* methicillin-susceptible *S. epidermidis, S. saprophyticus,* or vancomycin-susceptible *E. faecalis*.			✔ †				
Acute uncomplicated cystitis in females caused by *E. coli* or *S. saprophyticus*.			✔ ∞				
Acute uncomplicated cystitis caused by *C.diversus, Enterobacter aerogenes, E. coli, K. pneumoniae, P. mirabilis,* or *P. aeruginosa.*							✔ ∞
Chronic bacterial prostatitis caused *by E. coli* or *P. mirabilis.*			✔				
Chronic bacterial prostatitis caused *by E. coli, E. faecalis* or methicillin-susceptible *S. epidermidis.*						✔	
Prostatitis caused by *E. coli.*							✔
Infectious diarrhea caused by *E. coli* (enterotoxigenic isolates), *Campylobacter jejuni, Shigella boydii, Shigella dysenteriae, Shigella flexneri* or *Shigella sonnei*.			✔				
Typhoid fever (enteric fever) caused by *Salmonella typhi*.			✔				
Uncomplicated cervical and urethral gonorrhea caused by *Neisseria gonorrhoeae*.			✔				✔
Inhalational anthrax (post-exposure): To reduce the incidence or progression of disease following exposure to aerosolized *Bacillus anthracis*.			✔ ††			✔	
Plague caused by *Yersinia pestis* (treatment and prophylaxis).	✔		✔ ††			✔	
Urethritis and cervicitis caused by *Chlamydia trachomatis*							✔
Mixed infections of the urethra and cervix or pelvic inflammatory disease due to *N. gonorrhoeae and C. trachomatis.*							✔

* Multi-drug resistant isolates

[∫] Also indicated for *H. parainfluenzae* and *Legionella pneumophilia*. Also indicated for nosocomial pneumonia caused by methicillin-susceptible *S. aureus*, *P. aeruginosa*, *S. marcescens, E. coli, K. pneumoniae, H. influenzae*, or *S. pneumoniae*. Adjunctive therapy should be used as clinically indicated. Where *P. aeruginosa* is a documented or presumptive pathogen, combination therapy with an anti-pseudomonal β-lactam is recommended.
[‡] Not indicated for *K. pneumoniae* or methicillin-susceptible *S. aureus.*
[‡‡] Not indicated for methicillin-susceptible *S. aureus.*
[ǂ] Not indicated for *K. pneumoniae*.
[ǂǂ] Also indicated for *E. cloacae.*
[**] Ciprofloxacin is not a drug of first choice in the treatment of presumed or confirmed pneumonia secondary to *S. pneumoniae.*
[†] Complicated urinary tract infections and pyelonephritis due to *E. coli* for children one to 17 years but not drug of first choice.
[††] For adults and children
∞ Reserve for use in patients who have no alternative treatment options.

(Prescribing information: Avelox, 2016; Baxdela, 2017; Cipro, 2016; Ciprofloxacin extended release tablet, 2016; Factive, 2016; Levaquin, 2017; Ofloxacin, 2016)

- Information on indications, mechanism of action, pharmacokinetics, dosing, and safety has been obtained from the prescribing information for the individual products, except where noted otherwise.

CLINICAL EFFICACY SUMMARY

- The efficacy of the fluoroquinolones has been well documented in the treatment of genitourinary, respiratory, dermatological, and other miscellaneous infections, including typhoid fever and complicated intra-abdominal infections.
- A meta-analysis demonstrated no significant differences in clinical or microbiological efficacy between the quinolones for the treatment of acute cystitis (Rafalsky et al, 2006). Another meta-analysis found no difference between fluoroquinolones and other classes of antibiotics for uncomplicated cystitis with regard to symptomatic cure (Zalmanovici-Trestioreanu et al, 2010). For the treatment of urinary tract infections, two randomized clinical trials were conducted that directly compared the once-daily, extended-release formulation of ciprofloxacin with the equivalent dose of the twice-daily immediate release formulation (Fourcroy et al, 2005; Talan et al, 2004). Overall, the extended-release formulation was found to provide comparable bacteriological eradication rates and/or clinical cure rates as the immediate-release formulation with comparable rates of adverse reactions.
- Several head-to-head trials have demonstrated no significant differences between fluoroquinolone agents for the treatment of urinary tract infections (Arredondo-Garcia et al, 2004; Auquer et al, 2002; Peterson et al, 2008; Raz et al, 2000; Richard et al, 2008; Schaeffer et al, 1992). In one study, cefpodoxime did not demonstrate non-inferiority versus ciprofloxacin in the treatment of acute cystitis (Hooten et al, 2012).
- Both levofloxacin and ciprofloxacin have demonstrated efficacy in the treatment of bacterial prostatitis (Bundrick et al, 2003; Naber et al, 2008). In a meta-analysis, no fluoroquinolone demonstrated consistent superiority over another for the treatment of chronic bacterial prostatitis (Perletti et al, 2013).
- Four meta-analyses have been conducted comparing quinolones to other antibiotics for the treatment of acute sinusitis and community-acquired pneumonia (Karageorgopoulos et al, 2008; Salkind et al, 2002; Varadakas et al, 2008; Raz-Pasteur et al, 2015). Results from these analyses established the efficacy of the quinolones in respiratory infections. When compared to other antibiotics (β-lactams, macrolides, β-lactams/macrolide combination therapy, doxycycline, or a ketolide), treatment with quinolones was generally clinically comparable or superior. However, the majority of trials assessed in the meta-analysis by Salkind et al included sparfloxacin, trovafloxacin, and grepafloxacin, which are not currently available in the United States. In another meta-analysis, gemifloxacin was shown to have a higher treatment success rate than other fluoroquinolones and similar rates to β-lactams and macrolides in the treatment of community-acquired pneumonia and acute exacerbations of chronic bronchitis (Zhang et al, 2012). Eradication rates were similar between gemifloxacin and other fluoroquinolones, β-lactams, and macrolides.
- A meta-analysis in patients with acute COPD exacerbations did not find a consistent significant benefit of antibiotics across outcomes with the exception of patients admitted to the intensive care unit (Vollenweider et al, 2012).
- For patients with skin and skin structure infections, two trials demonstrated similar clinical success and eradication rates with levofloxacin and ciprofloxacin (Nichols et al, 1997; Nicodemo et al, 1998). Additionally, results from clinical trials

have revealed similar cure rates for delafloxacin compared to tigecycline, linezolid, and the combination of vancomycin/aztreonam in the treatment of acute bacterial skin and skin structure infections (O'Riordan et al 2015; Kingsley et al, 2016; O'Riordan et al, 2016).

- A meta-analysis of four randomized, controlled trials evaluated moxifloxacin versus other combination antibiotic regimens for the treatment of intra-abdominal infections (Mu et al, 2012). This analysis showed that moxifloxacin had similar clinical cure rates, bacteriological success rates, and mortality compared with those of the control group.

CLINICAL GUIDELINES

- Treatment guidelines for the treatment of community-acquired pneumonia, urinary tract infections, skin and soft tissue infections, and vertebral osteomyelitis recommend fluoroquinolones as alternative agents (Berbari et al, 2015; Chow et al, 2012; Gupta et al, 2011; Mandell et al, 2007; Snellman et al, 2013; Stevens et al, 2014).
- Fluoroquinolones should be considered first-line therapy for bacterial prostatitis, inhalational anthrax, and some types of infectious diarrhea (Guerrant et al, 2001; Stern et al, 2008).
- The Centers for Disease Control and Prevention has determined that fluoroquinolones should no longer be used for the treatment of gonorrhea due to resistant organisms. They are not recommended for routine use in pelvic inflammatory disease unless antimicrobial susceptibility testing is performed and the fluoroquinolone will be administered in combination with metronidazole (CDC, 2015).

SAFETY SUMMARY

- All fluoroquinolones carry a boxed warning for disabling and potentially irreversible serious adverse reactions from different body systems that can occur together in the same patient. Commonly observed adverse reactions include tendinitis, tendon rupture, arthralgia, myalgia, peripheral neuropathy, and central nervous system effects (ie, hallucinations, anxiety, depression, insomnia, severe headaches, confusion).
  - The risk for fluoroquinolone-associated tendinitis and tendon rupture is increased in patients over 60 years of age, in patients taking corticosteroid drugs, and in patients with kidney, heart, or lung transplants.
- Due to the potentially permanent serious adverse events involving the tendons, muscles, joints, nerves, and central nervous system, the FDA published a safety communication which recommends reserving the use of fluoroquinolones in acute sinusitis, acute bronchitis, and uncomplicated urinary tract infections for patients with no alternative treatment options (FDA press release, 2016). A subsequent safety alert released by the FDA stated that after review, it did not find that use of fluoroquinolones resulted in detached retina, aortic aneurysm, or aortic dissection (FDA press release, 2017).
- Fluoroquinolones may cause QT interval prolongation, anaphylactic reactions, phototoxicity, *Clostridium difficile* diarrhea, blood glucose disturbances. Additionally, fluoroquinolones may exacerbate muscle weakness in patients with myasthenia gravis and should therefore be avoided.
- The most common adverse events with fluoroquinolones include gastrointestinal (eg, nausea, vomiting, diarrhea) and central nervous system (eg, dizziness, headache) toxicities. Rash is frequently observed with fluoroquinolones and is especially common with gemifloxacin.
- All fluoroquinolones bind to multivalent cations. Administration of a fluoroquinolone should be separated by at least two hours from products containing aluminum, magnesium, iron, or zinc.
- Additional drug interactions include Class IA and Class III antiarrhythmics, nonsteroidal anti-inflammatory drugs, phenytoin, probenecid, sulfonylureas, theophylline, tizanidine, and warfarin.
- Oral dosing of ciprofloxacin, gemifloxacin, levofloxacin, and ofloxacin should be adjusted in renal impairment. Delafloxacin is not recommended for use in patients with end stage renal disease. The daily dose of ofloxacin should not exceed 400 mg in patients with severe liver dysfunction.

DOSING AND ADMINISTRATION

Table 3. Dosing and Administration

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Avelox (moxifloxacin)*,†	Tablet	Oral	Every 24 hours	
Baxdela (delafloxacin)*	Tablet	Oral	Every 12 hours	Not recommended in ESRD (eGFR <

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
				15 including hemodialysis)
Cipro (ciprofloxacin)*,†	Tablet, suspension	Oral	Every 12 hours	Oral dose adjustments are recommended in renal impairment. Ofloxacin dose should not exceed 400 mg per day in patients with severe liver dysfunction disorders.
ciprofloxacin extended release	Tablet	Oral	Every 24 hours	
Factive (gemifloxacin)	Tablet	Oral	Every 24 hours	
Levaquin (levofloxacin)* ,†	Tablet, oral solution	Oral	Every 24 hours	
ofloxacin†	Tablet	Oral	Every 12 hours	

Abbreviations: eGFR = estimated glomerular filtration rate; ESRD = end stage renal disease
* Also available as intravenous solution
† Also available as otic and/or ophthalmic formulations
See the current prescribing information for full details

CONCLUSION

- Fluoroquinolones have a broad spectrum of activity and may be used to treat a variety of infections. Current clinical evidence supports the efficacy of all products in this class for their FDA-approved indications, and efficacy appears comparable among agents. No fluoroquinolone has consistently demonstrated superiority over another.
- Fluoroquinolones should be considered first-line therapy for bacterial prostatitis, inhalational anthrax, and some types of infectious diarrhea (Stern et al, 2008; Guerrant et al, 2001).
  - Treatment guidelines recommend fluoroquinolones as alternative agents for the treatment of community-acquired pneumonia, urinary tract infections, skin and soft tissue infections, and vertebral osteomyelitis (Berberi et al, 2015; Gupta et al, 2011; Mandell et al, 2007; Solomkin et al, 2010; Stevens et al, 2014). They are not generally recommended for the treatment of bacterial sinusitis (Chow et al, 2012; Snellman et al, 2013). The Centers for Disease Control and Prevention has determined that fluoroquinolones should no longer be used for the treatment of gonorrhea due to resistant organisms (CDC, 2015).
- All fluoroquinolones share a boxed warning for disabling and potentially irreversible serious adverse reactions such as tendinitis, tendon rupture, arthralgia, myalgia, peripheral neuropathy, and central nervous system effects (ie, hallucinations, anxiety, depression, insomnia, severe headaches, confusion). Due to the risk for permanent adverse effects, the FDA warns that fluoroquinolones should be reserved for patients with no other treatment options when used to treat acute sinusitis, acute bronchitis, and uncomplicated urinary tract infections (FDA press release, 2016).
- Additional warnings for the class include QT prolongation, blood glucose disturbances, *Clostridium difficile*-associated diarrhea, and phototoxicity. Fluoroquinolones should be avoided in patients with a history of myasthenia gravis.

REFERENCES

- Arredondo-Garcia JL, Figueroa-Damian R, Rosas A, et al. Comparison of short-term treatment regimen of ciprofloxacin versus long-term treatment regimens of trimethoprim/sulfamethoxazole or norfloxacin for uncomplicated lower urinary tract infections: a randomized, multicentre, open-label, prospective study. J Antimicrob Chemother. 2004;54(4):840-3.
- Auquer F, Cordon F, Gorina E, et al; the Urinary Tract Infection Study Group. Single-dose ciprofloxacin versus 3 days of norfloxacin in uncomplicated urinary tract infections in women. Clin Microbiol Infect. 2002;8(1):50-4.
- Avelox prescribing information. Bayer HealthCare Pharmaceuticals, Inc. Whippany, NJ. September 2016.
- Baxdela prescribing information. Melinta Therapeutics. Lincolnshire, IL. June 2017.
- Berbari EF, Kanj SS, Kowalski TJ, et al. 2015 Infectious Diseases Society of America (IDSA) Clinical Practice Guidelines for the Diagnosis and Treatment of Native Vertebral Osteomyelitis in Adults. Clin Infect Dis. 2015 September:e26-e46. Available from http://cid.oxfordjournals.org/content/61/6/e26.full.pdf+html. Accessed June 6, 2017.
- Bolon MK. The newer fluoroquinolones. Med Clin N Am. 2011; 95: 793–817.
- Bundrick W, Heron SP, Ray P, et al. Levofloxacin versus ciprofloxacin in the treatment of chronic bacterial prostatitis: a randomized double-blind multicenter study. Urology. 2003 Sep;62(3):537-41.
- Centers for Disease Control and Prevention (CDC). Plague: Resources for Clinicians. 2015. (content on the internet). Available from http://www.cdc.gov/plague/healthcare/clinicians.html. Accessed June 6, 2017.
- Centers for Disease Control and Prevention (CDC). Sexually transmitted diseases treatment guidelines, 2015. Available from: http://www.cdc.gov/std/tg2015/tg-2015-print.pdf. Accessed June 6, 2017.
- Chow AW, Benninger MS, Brook I, et al. IDSA Clinical Practice Guideline for Acute Bacterial Rhinosinusitis in Children and Adults. Clin Infect Dis. 2012 May:e1-e41. Available from https://www.idsociety.org/uploadedFiles/IDSA/Guidelines-

Patient_Care/PDF_Library/IDSA%20Clinical%20Practice%20Guideline%20for%20Acute%20Bacterial%20Rhinosinusitis%20in%20Children%20and%20Adults.pdf. Accessed June 6, 2017.
- Cipro prescribing information. Bayer HealthCare Pharmaceuticals Inc. Whippany, NJ. September 2016.
- Ciprofloxacin extended release tablet prescribing information. Mylan Pharmaceuticals Inc. Morgantown, WV. August 2016.
- Drugs@FDA [database on the Internet]. Rockville (MD): Food and Drug Administration (US), Center for Drug Evaluation and Research; 2017. Available from: https://www.accessdata.fda.gov/scripts/cder/daf/. Accessed June 5, 2017.
- Factive prescribing information. Merus Labs. Toronto, ON, Canada. May 2016.
- Food and Drug Administration (FDA) Drug Safety Communication. FDA updates warnings for oral and injectable fluoroquinolone antibiotics due to disabling side effects. [press release]. July 26, 2016 Available at: http://www.fda.gov/Drugs/DrugSafety/ucm511530.htm. Accessed June 6, 2017.
- Food and Drug Administration (FDA) Drug Safety Communication. Fluoroquinolone antibacterial drugs for systemic use: drug safety communication – warnings updated due to disabling side effects. [press release]. May 10, 2017. Available at: https://www.fda.gov/safety/medwatch/safetyinformation/safetyalertsforhumanmedicalproducts/ucm513065.htm. Accessed June 5, 2017.
- Fourcroy JL, Berner B, Chiang YK, et al. Efficacy and safety of a novel once-daily extended-release ciprofloxacin tablet formulation for treatment of uncomplicated urinary tract infection in women. Antimicrob Agents Chemother. 2005;49(10):4137-43.
- Guerrant RL, Van Gilder T, Steiner TS, et al; Infectious Diseases Society of America. Practice guidelines for the management of infectious diarrhea. Clin Infect Dis. 2001;32:331-51.
- Gupta K, Hooton TM, Naber KG, et al.; Infectious Diseases Society of America; European Society for Microbiology and Infectious Diseases. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: A 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. Clin Infect Dis. 2011 Mar;52(5):e103-20.
- Hooten TM, Roberts PL, Stapleton AE. Cefpodoxime vs ciprofloxacin for short-course treatment of acute uncomplicated cystitis. A randomized trial. JAMA. 2012;307(6):583-5-89.
- Karageorgopoulos DE, Giannopoulou KP, Grammatikos AP, et al. Fluoroquinolones compared with β-lactam antibiotics for the treatment of acute bacterial sinusitis: a meta-analysis of randomized controlled trials. CMAJ. 2008;178(7):845-54.
- Kingsley J, Mehra P, Lawrence LE, et al. A randomized, double-blind, Phase 2 study to evaluate subjective and objective outcomes in patients with acute bacterial skin and skin structure infections treated with delafloxacin, linezolid or vancomycin. J Antimicrob Chemother. 2016;71(3):821-829.
- Levaquin prescribing information. Janssen Pharmaceuticals, Inc. Titusville, NJ. February 2017.
- Mandell LA, Wunderink RG, Anzueto A, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis. 2007 Mar 1;44 Suppl 2:S27-72.
- Mu YP, Liu RL, Wang LQ, et al. Moxifloxacin monotherapy for treatment of complicated intra-abdominal infections: a meta-analysis of randomised controlled trials. Int J Clin Pract. 2012 Feb;66(2): 210–17.
- Naber KG, Roscher K, Botto H, et al. Oral levofloxacin 500 mg once daily in the treatment of chronic bacterial prostatitis. Int J Antimicrob Agents. 2008;32:145-53.
- Nichols RL, Smith JW, Gentry LO, et al. Multicenter, randomized study comparing levofloxacin and ciprofloxacin for uncomplicated skin and skin structure infections. South Med J. 1997;90(12):1193-200.
- Nicodemo AC, Robledo JA, Jasovich A et al. A multicenter, double-blind, randomized study comparing the efficacy and safety of oral levofloxacin versus ciprofloxacin in the treatment of uncomplicated skin and skin structure infections. Int J Clin Pract. 1998;52(2):69-74.
- O'Riordan W, McManus A, Teras J, et al. A global phase 3 study of delafloxacin compared to vancomycin/aztreonam in patients with acute bacterial skin and skin structure infections. Open Forum Infect Dis. 2016;3(Suppl 1):1347.
- O'Riordan W, Mehra P, Manos P, et al. A randomized phase 2 study comparing two doses of delafloxacin with tigecycline in adults with complicated skin and skin-structure infections. Int J Infect Dis. 2015;30:67-73.
- Ofloxacin prescribing information. Larken Laboratories. Canton, MS. July 2016.
- Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations [database on the internet]. Silver Spring, MD: Food and Drug Administration (US), Center for Drug Evaluation and Research; 2017. Available at http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Accessed June 5, 2017.
- Perletti G, Marras E, Wagenlehner FME, et al. Antimicrobial therapy for chronic bacterial prostatitis. Cochrane Database Syst Rev. 2013;8:CD009071.
- Peterson J, Kaul S, Khashab M, et al. A double-blind, randomized comparison of levofloxacin 750 mg once-daily for five days with ciprofloxacin 400/500 mg twice-daily for 10 days for the treatment of complicated urinary tract infections and acute pyelonephritis. Urology. 2008;71(1):17-22.
- Rafalsky V, Andreeva I, Rjabkova E. Quinolones for uncomplicated acute cystitis in women. Cochrane Database Syst Rev. 2006 Jul 19;3:CD003597.
- Raz R, Naber KG, Raizenberg C, et al. Ciprofloxacin 250 mg twice daily versus ofloxacin 200 mg twice daily in the treatment of complicated urinary tract infections in women. Eur J Clin Microbiol Infect Dis. 2000;19(5):327-31.
- Raz-Pasteur A, Shasha D, Paul M. Fluoroquinolones or macrolides alone versus combined with β-lactams for adults with community-acquired pneumonia: Systematic review and meta-analysis. Int J Antimicrob Agents. 2015;46(3):242-8.
- Richard GA, Klimberg IN, Fowler CL, et al. Levofloxacin versus ciprofloxacin versus lomefloxacin in acute pyelonephritis. Urology. 1998;52(1):51-5.
- Salkind AR, Cuddy PG, Foxworth JW. Fluoroquinolone treatment of community-acquired pneumonia: a meta-analysis. Ann Pharmacother. 2002;36(12):1938-43.
- Schaeffer AJ, Anderson RU. Efficacy and tolerability of norfloxacin vs ciprofloxacin in complicated urinary tract infection. Urology. 1992;40(5):446-9.
- Snellman L, Adams W, Anderson G, et al. Institute for Clinical Systems Improvement. Diagnosis and Treatment of Respiratory Illness in Children and Adults. Update 2013 January. Available at https://www.icsi.org/_asset/1wp8x2/RespIllness.pdf. Accessed June 6, 2017.
- Solomkin JS, Mazuski JE, Bradley JS, et al. Diagnosis and management of complicated intra-abdominal infection in adults and children: guidelines by the Surgical Infection Society and the Infectious Diseases Society of America. Surg Infect (Larchmt). 2010 Feb;11(1):79-109.
- Stern EJ, Uhde KB, Shadomy SV, et al. Conference report on public health and clinical guidelines for anthrax [conference summary]. Emerg Infect Dis [serial on the Internet]. 2008 Apr. Available from http://wwwnc.cdc.gov/eid/article/14/4/07-0969.htm. Accessed June 6, 2017.
- Stevens DL, Bisno AL, Chambers HF, et al. Practice guidelines for the diagnosis and management of skin and soft-tissue infections: 2014 update by the Infectious Diseases Society of America. Clin Infect Dis. 2014;59(2):e10-e52.

- Talan DA, Klimberg IW, Nicolle LE, et al. Once daily, extended release ciprofloxacin for complicated urinary tract infections and acute uncomplicated pyelonephritis. J Urol. 2004;171(2 Pt 1):734-9.
- Varadakas KZ, Siempos II, Grammatikos A, et al. Respiratory fluoroquinolones for the treatment of community-acquired pneumonia: a meta-analysis of randomized controlled trials. CMAJ. 2008;179(12):1269-77.
- Vollenweider DJ, Jarrett H, Steurer-Stey CA, et al. Antibiotics for exacerbations of chronic obstructive pulmonary disease (review). Cochrane Database Syst Rev. 2012;12:CD010257.
- Zalmanovici-Trestioreanu A, Green H, Paul M, et al. Antimicrobial agents for treatment uncomplicated urinary tract infection in women (review). Cochrane Database Syst Rev. 2010;10:CD007182.
- Zhang L, Wang R, Matthew FE, et al. Gemifloxacin for the treatment of community-acquired pneumonia and acute exacerbation of chronic bronchitis: a meta-analysis of randomized controlled trials. Chin Med J. 2012;125(4): 687-95 .

Publication Date: June 27, 2017