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CME

# Improving the Safe Use of Fluoroquinolone Antibiotics

# Introduction

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Fluoroquinolones are potent broad-spectrum bactericidal drugs that have been widely used in medical practice since the 1970s to treat a variety of infectious diseases.<sup>[1]</sup> They exert their antibacterial effect by inhibiting one or more bacterial topoisomerase enzymes, thus preventing bacterial DNA from unwinding, separating and duplicating.<sup>[2,3]</sup> Five fluoroquinolones are currently marketed and approved by the United States Food and Drug Administration (FDA) for systemic use<sup>[4-8]</sup>:

- Ciprofloxacin: systemic forms available include tablets, oral suspension, and injection
- Ofloxacin: systemic forms available include tablets and injection
- Levofloxacin: systemic forms available include tablets, oral suspension, and injection
- Moxifloxacin: systemic forms available include tablets and injection
- Gemifloxacin: available in tablet form for systemic use

Their efficacy against a wide range of Gram-positive and Gram-negative pathogenic bacteria has led to their widespread use.<sup>[1]</sup> By 2002, fluoroquinolones were the most commonly prescribed antibacterial class in adults,<sup>[9]</sup> often for conditions that do not always require antibacterial therapy, including acute bacterial sinusitis (ABS), mild acute bacterial exacerbation of chronic bronchitis (ABECB), and uncomplicated urinary tract infection (uUTI). Each year, an estimated 22 to 23 million unique patients receive prescriptions for oral systemic fluoroquinolones dispensed from outpatient retail pharmacies in the United States.<sup>[10]</sup> The most frequent prescribers are physicians in family medicine (20.5%) and internal medicine (19.2%), while nurse practitioners and physician assistants account for 9.8% and 8.2% of these prescriptions, respectively.

<sup>[10]</sup>Inappropriate use of fluoroquinolones encourages the development and spread of multi-drug-resistant bacteria, the proliferation of *Clostridium difficile*, and may unnecessarily subject patients to serious adverse events (AEs) associated with these antibiotics. Due to safety signals that have emerged over the lifecycle of these drugs, the FDA undertook a review of the risks and benefits of fluoroquinolones when used for ABS, ABECB, and uUTI.

This article reviews the overuse and misuse of fluoroquinolones in patients with these conditions; the relative efficacy and safety of fluoroquinolones for the treatment of ABS, ABECB, and uUTI; and revisions to the product labels for fluoroquinolones approved for use in the United States.

## Adverse Events (AEs) Associated With Fluoroquinolones

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Drug-related AEs are an under-appreciated consequence of fluoroquinolone use. A recent review by the FDA of the use of systemic fluoroquinolones to treat ABS, ABECB, and uUTI identified a constellation of serious, and sometimes life-altering, AEs, which resulted in important updates to safety information in the product labels. The FDA states that, "We have determined that fluoroquinolones should be reserved for use in patients who have no other treatment options for ABS, ABECB, and uUTIs because the risk of serious side effects generally outweighs the benefits in these patients. For some serious bacterial infections, the benefits of fluoroquinolones outweigh the risks, and it is appropriate for them to remain available as a therapeutic option."<sup>[11]</sup> A summary of the findings of the review follows.

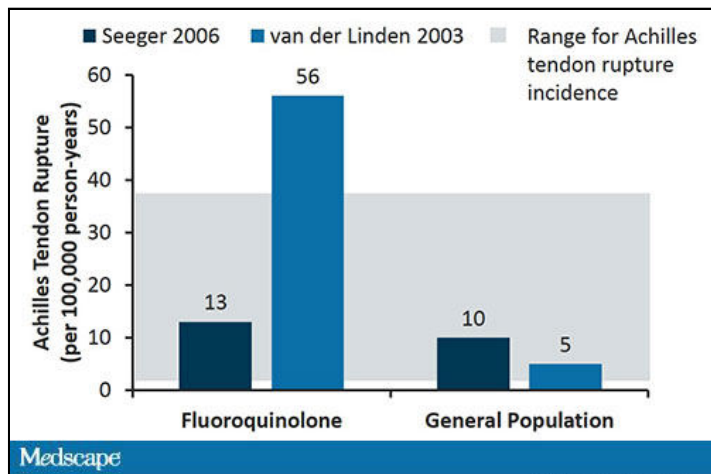
The serious AEs that are associated with fluoroquinolones include tendinopathy (eg, tendinitis and tendon rupture), peripheral neuropathy, central nervous system effects (eg, hallucinations, anxiety, depression, insomnia, severe headaches, and confusion), arthralgias, and myalgias. Worsening of preexisting myasthenia gravis, peripheral neuropathy, and cardiac (including QT interval prolongation and torsades de pointes) and dermatologic adverse events (eg, toxic epidermal necrolysis, Stevens-Johnson syndrome) can also occur.<sup>[4-</sup>

<sup>8]</sup>Data from the FDA Adverse Event Reporting System (FAERS) show that symptoms of these AEs can interfere with patients' ability to perform activities of daily living and can have a major impact on their quality of life.<sup>[10]</sup> A discussion of some of the more frequent or serious AEs follows.

## Tendinopathy

Numerous clinical studies have consistently found that fluoroquinolones are associated with an increased risk of tendinitis and tendon rupture, observed in, but not limited to, the Achilles tendon (Figure 1).<sup>[12-14]</sup> In a report on more than 11,000 patients, the rates for tendinitis were 2.4 per 10,000 patient prescriptions and 1.2 per 10,000 prescriptions for tendon rupture.<sup>[13]</sup> Symptoms have been reported as early as 2 hours after the initial drug exposure and as late as 6 months after discontinuation of the drug.<sup>[10]</sup>

**Figure 1. Frequency of Achilles tendon rupture in patients using fluoroquinolones compared with the general population.<sup>[10]</sup>**



Although tendinopathy related to fluoroquinolone use has occurred in all age groups, patients who are >60 years of age are at significant risk. One case series showed that 17% of all patients reporting tendinopathy were 60 years of age or older, a 3-fold increase over people without fluoroquinolone exposure.<sup>[10]</sup> Other risk factors for tendinopathy include rheumatoid arthritis, recent exposure to topical or systemic corticosteroid therapy, renal failure, solid organ transplantation (eg, kidney, heart, and lung), and strenuous physical activity during or immediately after treatment.<sup>[10]</sup>

## Peripheral Neuropathy

Post-marketing surveillance data<sup>[10]</sup> and numerous published case reports spanning 2 decades<sup>[15-17]</sup> document drug-related peripheral neuropathy associated with fluoroquinolone treatment. The epidemiological evidence reviewed by the FDA did not assess onset or irreversibility of fluoroquinolone-associated peripheral neuropathy.<sup>[10]</sup> Symptoms of peripheral neuropathy can include numbness, tingling, paresthesiae, muscle weakness, and allodynia.<sup>[18]</sup>

### **Central Nervous System Effects**

The accumulation of post-marketing clinical evidence along with elucidation of the mechanism for fluoroquinolone-mediated central nervous system toxicity (inhibition of GABA<sub>A</sub> receptors in addition to activation of excitatory NMDA receptors) led to class-labeling for all fluoroquinolones. Central nervous system and psychiatric adverse reactions associated with fluoroquinolones, including increased intracranial pressure and psychosis, were included as a Boxed Warning in all fluoroquinolone labels. In 2011, pseudotumor cerebri was added as another serious central nervous system adverse reaction.<sup>[10]</sup>

### **Other Serious Adverse Reactions**

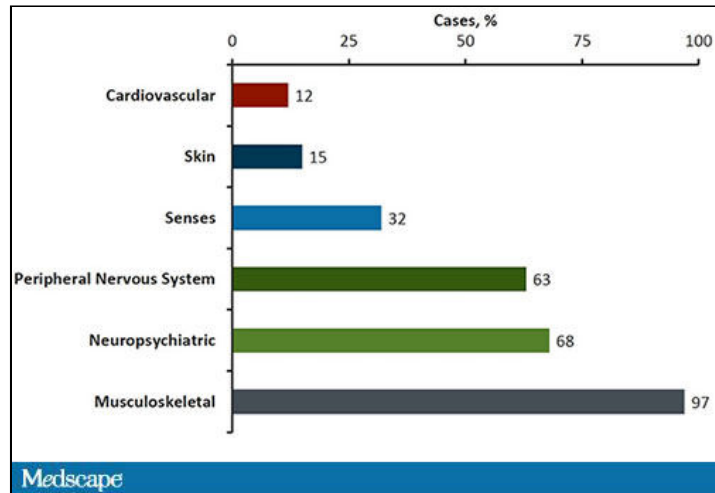
Exacerbation of myasthenia gravis were observed in some cases in premarketing clinical trials of fluoroquinolones, as well as postmarketing adverse reactions. A Boxed Warning was added to all fluoroquinolone labels to describe the potentially life-threatening consequences of exacerbation in patients with myasthenia gravis; healthcare professionals are advised to avoid use of fluoroquinolones in such patients. Drug-associated QT interval prolongation and Torsade de Pointes have been associated with fluoroquinolones and are included as Warnings for all fluoroquinolones. All fluoroquinolone labels provide a list of hypersensitivity reactions, including some reactions, such as anaphylaxis, that can have a fatal outcome.<sup>[10]</sup>

### **Disabling and Potentially Irreversible Serious Adverse Reactions**

A pattern of disabling and potentially permanent serious AEs involving the tendons, muscles, joints, nerves, and central nervous system can occur together in association with fluoroquinolone use.<sup>[10]</sup> A review of AE reports in the FDA Adverse Event Reporting System (FAERS) identified 1122 reports of disability in patients who were

healthy prior to taking an oral fluoroquinolone for uncomplicated sinusitis, bronchitis, or UTI.<sup>[10]</sup> A further analysis of AEs involving 2 or more body systems (eg, musculoskeletal, psychiatric, peripheral and central nervous system, skin, cardiovascular) that persisted at least 30 days after fluoroquinolone treatment ended, identified 178 cases (Figure 2).<sup>[10]</sup> The FAERS review found these cases associated with all of the systemic fluoroquinolones.<sup>[10]</sup> Most (74%) of the cases have been reported in patients 30 to 59 years of age.<sup>[10]</sup>

**Figure 2. Body systems affected in the 178 cases of disability identified in FAERS.<sup>[10]</sup>**



The constellation of symptoms (variably involving tendinopathy, muscle weakness, peripheral neuropathy, autonomic dysfunction, sleep disorders, cognitive dysfunction, and psychiatric disturbance) was recently described in a detailed presentation of 4 cases in which previously healthy adults without significant prior medical history each developed symptoms while being treated with a fluoroquinolone.<sup>[15]</sup> In all 4 patients, symptom progression continued even after they stopped taking the medication and persisted in varying degrees up to the time the case reports were published.

## Fluoroquinolones: Where Do They Fit in the Management of Patients With ABS, ABECB, and uUTI?

The benefits of fluoroquinolones can outweigh the risks when they are used in a treatment regimen for serious infections, such as pneumonia or intra-abdominal infections caused by fluoroquinolone-susceptible bacteria. However, in patients with ABS, mild ABECB, and uUTI, the risk of adverse events seems to outweigh potential benefits; thus, the FDA recommends that fluoroquinolones be used for these conditions only in patients who have no alternative treatment options, such as those with allergies or other known contra-indications to other antibacterial drugs.<sup>[19]</sup>

### **Fluoroquinolone Safety Labeling Changes in 2016**

For all systemic fluoroquinolones, the updated Boxed Warning in 2016 reflects the new safety information on serious adverse events including tendinitis, tendon rupture, peripheral neuropathy, and central nervous system effects. To minimize the risk for these serious AEs, the Boxed Warning includes the recommendation to reserve fluoroquinolones for use in patients who have no alternative treatment options for ABS, ABECB, and uUTI. The Boxed Warning for exacerbation of myasthenia gravis remains. This safety information is repeated in the Warnings and Precautions section of labeling.

In addition, the Indications and Usage section includes a limitation of use statement for the ABS, ABECB, and uUTI indications: “reserve for use in patients who have no alternative treatment options”, while the Information for Patients section and Medication Guide, which must be issued to a patient with each fluoroquinolone prescription, also includes the new safety information.

A 44-year-old woman who has a 20-pack-year history of cigarette smoking presents with a 10-day history of yellow-green nasal discharge, low-grade fever, and cough. She has tried over-the-counter decongestants without any improvement. She states that she has a

history of bacterial sinusitis, which has always been treated with antibiotics. She does not have any known sick contacts. She has no known drug allergies. On examination, she has a temperature of 102° F, maxillary tooth pain, and bilateral frontal and maxillary sinus pressure and pain. Her nasal turbinates are swollen and there is purulent nasal discharge. Her tympanic membranes are clear, her oropharynx is benign, and her neck has no lymphadenopathy. Her lungs are clear without wheezes, rales, or rhonchi. She has sinus tachycardia with a rate of 104 beats per minute. The diagnosis is ABS.

Which of the following antibiotics would you use to treat this patient?

None, I would not prescribe an antibiotic



Ciprofloxacin

Amoxicillin-clavulanate

Ceftazidime

Which of the following antibiotics would you use to treat this patient?

Your Peers Chose:

None, I would not prescribe an antibiotic	0%
Ciprofloxacin	0%
<input checked="" type="checkbox"/> Amoxicillin-clavulanate	0%
Ceftazidime	0%

This patient exhibits classic signs and symptoms of bacterial sinusitis and could be treated with amoxicillin-clavulanate for 10 days, as well as with other symptomatic treatments as needed, such as saline nasal rinses and decongestants.

Do not offer a fluoroquinolone, like ciprofloxacin, because the patient has other antibiotic treatment options available.

### **Management of Acute Bacterial Sinusitis**

Acute sinusitis (synonymous with acute rhinosinusitis) is symptomatic inflammation of the nasal cavity and paranasal sinuses lasting less than 4 weeks. The most common etiology is a viral infection, and acute viral sinusitis typically resolves spontaneously within 7 to 10 days; treatment in these cases is focused on symptomatic management and observation. Bacteria cause up to 2% of acute sinusitis episodes and ABS may also be a self-limited disease,<sup>[20]</sup> with up to 80% of immunocompetent patients improving within 2 weeks without antibiotic therapy.

<sup>[21]</sup>However, it can be difficult to differentiate viral from bacterial sinusitis and it is important for the patient and healthcare provider to recognize that antibiotic therapy may not be appropriate for many patients with signs and symptoms of acute sinusitis. Persistent symptoms or signs lasting for  $\geq 10$  days without clinical improvement, onset with severe symptoms, high fever, purulent nasal discharge or

facial pain and worsening symptoms or signs with new fever, headache or increased nasal discharge following a typical viral upper respiratory infection can help to identify patients with bacterial sinusitis.<sup>[22]</sup> In these patients, initial empiric treatment may consist of amoxicillin or amoxicillin-clavulanate. Macrolides and oral second- or third-generation cephalosporins are not generally recommended as first-line agents due to variable rates of resistance in *Streptococcus pneumoniae*, but can be utilized in patients with allergies to penicillins<sup>[23]</sup>, as can doxycycline.<sup>[22]</sup>

A review of 20 placebo-controlled trials showed limited evidence of benefit with fluoroquinolone use in patients with ABS. Fourteen studies failed to show a statistically significant difference in outcomes for antibacterial treatment compared with placebo; in each of the 6 studies that did show statistically significant differences, the primary efficacy outcome was different.<sup>[10]</sup> A Cochrane review of antibiotic therapy for clinically diagnosed acute rhinosinusitis in adults found that antibiotics can shorten the time to cure, but at any time point between 7 and 14 days, only 5 more participants per 100 would be cured faster if they receive an antibiotic vs placebo.<sup>[24]</sup> Taking into account the potential for antibiotic resistance and the low incidence of serious complications with this condition, the authors concluded that

there was no place for antibiotics in the treatment of healthy adult patients with clinically diagnosed, uncomplicated acute rhinosinusitis.<sup>[10,24]</sup>

A meta-analysis of data from 9 trials in which 2547 patients with rhinosinusitis-like complaints were randomly assigned to treatment with an antibiotic vs. placebo found that 15 patients would have to be treated with an antibiotic before 1 patient was cured.<sup>[25]</sup> Although there was some evidence for increased benefit with antibiotics in patients with purulent drainage in the pharynx, 8 patients with this physical sign would need to be treated before 1 additional patient was cured. In general, patients reporting more severe symptoms were not necessarily more likely to benefit from antibiotic therapy. The researchers caution however, that prompt treatment with antibiotics is indicated in patients with signs and symptoms of a serious infection or a complication such as high fever, periorbital swelling or erythema, and intense maxillary facial or tooth pain. The FDA concluded that the benefit of fluoroquinolones has been observed only in patients with prolonged and more severe symptoms, and the statistically significant difference from placebo is "not robust."<sup>[10]</sup>

A 65-year-old man with a past medical history significant for chronic obstructive pulmonary

disease (COPD) presents with a week-long history of progressive cough, now productive of clear to yellow phlegm. He has had a low-grade fever and wheezing that has gotten worse over the past 24 hours. He reports that during the past week he has experienced mild shortness of breath and is still smoking a pack of cigarettes a day. He is up to date on his influenza and pneumonia immunizations. On examination he has a temperature of 101° F but other vital signs are normal. An examination of the head, eyes, ears, nose, throat, and neck is unremarkable. His cough is productive and lung examination detects some diffuse wheezes which nearly clear after he coughs. He has a regular heart rate and rhythm. The diagnosis is ABECB superimposed on COPD.

Which of the following antibiotics would you use to treat this patient?

- None, I would not prescribe an antibiotic
- Azithromycin

Levofloxacin

Trimethoprim/sulfamethoxazole

Which of the following antibiotics would you use to treat this patient?

Your Peers Chose:

None, I would not prescribe an antibiotic	0%
<input checked="" type="checkbox"/> Azithromycin	0%
Levofloxacin	0%
Trimethoprim/sulfamethoxazole	0%

This patient has signs and symptoms of acute bacterial exacerbation of chronic bronchitis (ABECB) and can be offered an antibiotic. Azithromycin for 5 days is a reasonable choice in this setting; do not offer a fluoroquinolone, such as levofloxacin, because the patient has other treatment options available.



## Management of Acute Bronchitis and Acute Exacerbations of Chronic Bronchitis

Acute bronchitis and acute exacerbation of chronic bronchitis (AECB) are often treated with antibacterials; nearly 75% of all antibacterials are prescribed for these conditions.<sup>[26]</sup> Acute bronchitis can occur in patients with no prior lung disease, is characterized by self-limited inflammation of the upper bronchi due to airway infection, and the majority of these episodes are caused by respiratory viruses.<sup>[27]</sup> Patients typically experience an acute-onset cough lasting 1 to 3 weeks, which may or may not be associated with sputum production. AECB, also commonly referred to as chronic obstructive pulmonary disease (COPD) exacerbation, is defined as an acute worsening of 1 or more cardinal respiratory symptoms (increased cough [frequency or severity], sputum [purulence or production], or dyspnea beyond normal day-to-day variations) resulting in the need to change the patient's medication.<sup>[28]</sup>

The production of purulent sputum in patients with AECB often indicates a greater likelihood of bacterial infection (ABECB).<sup>[28]</sup> Antibacterial therapy is recommended for patients with moderate-to-severe exacerbations, defined as having all 3 cardinal

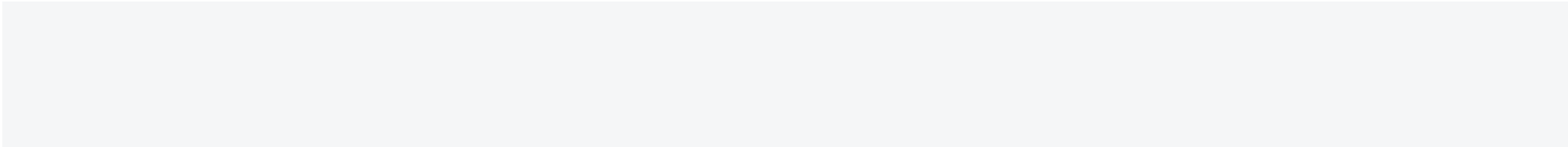
symptoms, or 2 cardinal symptoms with purulent sputum, or needing mechanical ventilation. Respiratory fluoroquinolones should be avoided if possible. In a review of 15 placebo-controlled studies of patients with varying degrees of severity of ABECB, 9 studies showed no difference in clinical outcomes between patients who received placebo and patients who received an antibacterial drug.<sup>[10]</sup> The other six studies also enrolled patients with varying disease severity, and using different outcome assessments, showed a statistically significant difference in favor of an antibacterial.<sup>[10]</sup> Eight studies included only outpatients; of these, 4 studies, which evaluated only patient-reported outcomes, showed a statistically significant difference in outcomes between antibiotic and placebo. The other 4 studies that did not show a difference used other outcome assessments, such as pulmonary function testing.<sup>[10]</sup>

A 23-year-old woman calls her primary care office with a complaint of an 1-day history of dysuria. She has no fever, no chills, and no history of UTI. She is sexually active and monogamous with her

husband. She is not pregnant. She has never had a sexually-transmitted infection. She takes no medication and has no allergies. The presumed diagnosis is uUTI.

Which of the following antibiotics would you use to treat this patient?

- None, I would not prescribe an antibiotic
- Moxifloxacin
- Bactrim DS
- Clindamycin



Which of the following antibiotics would you use to treat this patient?

Your Peers Chose:

None, I would not prescribe an antibiotic	0%
Moxifloxacin	0%
<input checked="" type="checkbox"/> Bactrim DS	0%
Clindamycin	0%

This patient has signs and symptoms of uncomplicated urinary tract infection. She should be treated with sulfamethoxazole and trimethoprim twice daily for 3 days and advised to follow-up for a urinalysis and culture if her symptoms do not improve. Do not use a fluoroquinolone because the patient has other antibiotic

treatment options; furthermore, moxifloxacin does not have an indication for treatment of uncomplicated urinary tract infection.

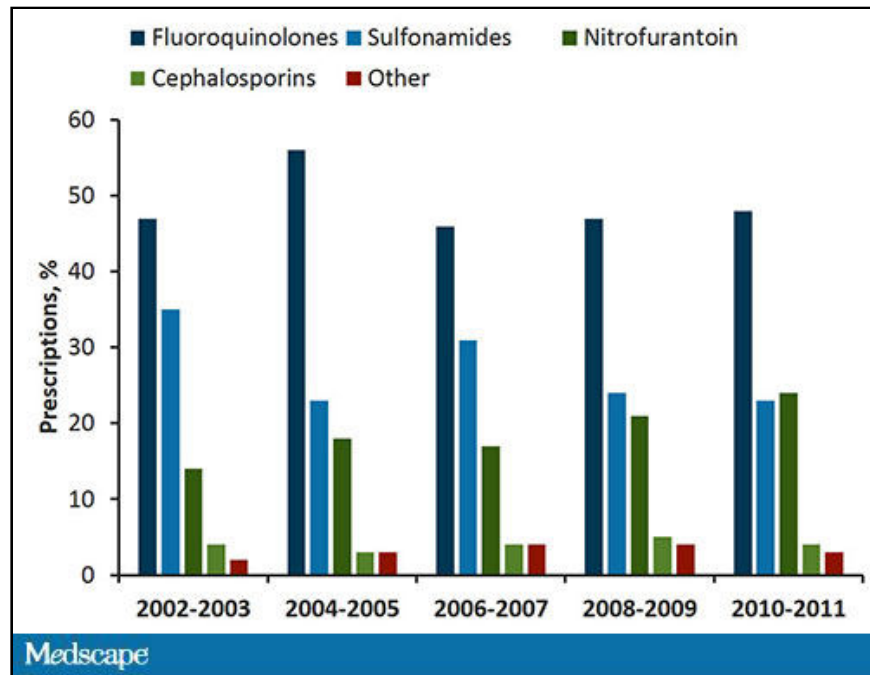
## Management of Uncomplicated UTI Infection

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Uncomplicated UTI is one of the most common outpatient diagnoses in the United States and one of the most common indications for prescribing antibacterials to otherwise healthy women in the community.<sup>[29]</sup> Uncomplicated UTI usually refers to acute cystitis (eg, infection of the bladder or lower urinary tract) in a non-pregnant woman with normal anatomy and no indwelling devices.

According to data from the National Ambulatory Medical Care and National Hospital Ambulatory Medical Care Survey, 80% of outpatient visits between 2002 and 2011 that involved an adult woman with a diagnosis of uUTI, resulted in an antibiotic prescription, and fluoroquinolones were the most frequently prescribed antibiotic class, in 49% of cases (Figure 3).<sup>[30]</sup>

**Figure 3. Percentage of US prescriptions for uncomplicated urinary tract infection, 2002-2011, by antibiotic class. Antibiotics included oral penicillins, cephalosporins, macrolides, fluoroquinolones, lincomycin derivatives, tetracyclines, sulfonamides, and nitrofurantoin.<sup>[30]</sup>**



In its 2015 review, the FDA identified 5 published controlled trials of antibiotic therapy for uUTI.<sup>[10]</sup> Four trials were placebo-controlled and 1 used ibuprofen as the control. The reviewers concluded that there was a clear and consistent treatment effect (microbiologic eradication) with antibiotic drug therapy for uUTI. In the

placebo-controlled trials, a treatment effect was also demonstrated when the outcome measure was symptom resolution. In the study that used ibuprofen as a control, there was no difference between treatment groups in terms of symptom resolution.>

Symptomatic or proven UTIs are usually treated with antibiotics; some however, may resolve in the absence of antibiotics. For example, a small prospective cohort study found that 37% of women with symptoms of uUTI were willing to delay antibacterial treatment after they were counseled by their doctor.<sup>[31]</sup> In this study, healthy, non-pregnant women who contacted their primary care physician with painful and/or frequent micturition for no longer than 7 days collected urine for urinalysis and culture. Physicians were instructed to ask all patients whether they were willing to delay antibiotic treatment, although they could opt to receive antibiotic therapy at any time later. After 1 week, patients were asked about the current status of their symptoms and whether they had used any antibiotics. Of the 28 women who were willing to delay treatment and who had not used antibiotics, 20 (71%) reported clinical improvement or cure.<sup>[31]</sup>

The type and duration of antibiotic therapy are dependent on patient history, allergies, involvement of the upper tract, severity of illness, and patient tolerance of



the drug.<sup>[29]</sup> The following agents are recommended as first-line therapy for treatment of uUTI<sup>[29]</sup>:

- Trimethoprim/sulfamethoxazole
- Nitrofurantoin monohydrate/macrocrystals
- Fosfomycin trometamol (lower efficacy than some other recommended agents; avoid if early pyelonephritis is suspected)

Notably, these treatment guidelines consider fluoroquinolones as second line treatment.

## Prescribing Fluoroquinolones

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The number of fluoroquinolone prescriptions written and dispensed in the United States is substantial. An examination of data from National Ambulatory Medical Care Surveys from 2006 through 2012 identified 93 million ambulatory visits in which a fluoroquinolone was prescribed.<sup>[32]</sup> A prescription was considered off-label when none of the visit diagnoses corresponded to an FDA-approved indication for

fluoroquinolone use; more than one-half of these prescriptions were found to have been written for off-label indications.<sup>[32]</sup>

Given the recent product label changes for fluoroquinolones, providers must rethink how they treat ABS, mild ABECB, and uUTI. The principles of appropriate prescribing of fluoroquinolones include careful patient selection, counseling patients about potential AEs, understanding the potential for the development of antibiotic resistance and the need for antibiotic stewardship; these will be covered in the following sections.<sup>[10,11]</sup>

### **Counseling Patients About AEs**

Patients who are treated with fluoroquinolones should be educated about possible AEs as discussed in the previous sections. Importantly, patients should know that these AEs can occur within hours to weeks after starting treatment with a fluoroquinolone.<sup>[19]</sup> When following up with patients, open-ended and specific questions designed to elicit recognition and reporting of AEs should be posed; for example:

- How are you taking your medication?

- Are you having any problems with this medication?
- Have you had any new pains in your joints or muscles?
- Have you had any tingling or numbness?

Patients should be advised to stop the drug, and contact a healthcare professional immediately if they experience a serious AE while taking a fluoroquinolone; a non-fluoroquinolone antibacterial may be prescribed to complete the treatment course. Fluoroquinolones should be avoided in patients who have previously experienced a serious AE associated with any drug in this class.<sup>[19]</sup>

### **Antibiotics: The More You Use Them, the Faster You Lose Them**

Antibacterial resistance can occur through a variety of mechanisms, and is an urgent concern worldwide.<sup>[1,33]</sup> The overuse of antibacterials is the single most important factor leading to resistance.<sup>[33]</sup> As bacteria become increasingly resistant to existing treatment options, resultant infections have become more difficult to treat. For example fluoroquinolone resistance in group B *Streptococcus*, *Escherichia*

*coli* and *Salmonella* sp. are increasingly worrisome.<sup>[34-36]</sup> Further, there has been a significant rise in *C. difficile* infections associated with fluoroquinolone use.<sup>[11]</sup>

Each year in the United States, at least 2 million people become infected with bacteria that are resistant to antibacterials.<sup>[33]</sup> Infections caused by resistant organisms can be difficult to treat and often require costly, and sometimes toxic, alternatives; at least 23,000 people in healthcare settings die each year as a direct result of these infections.<sup>[33]</sup> Antibiotic stewardship has emerged as a cornerstone to combating antibacterial drug resistance. The potential for antibacterial resistance should be considered when selecting therapy for every patient.

## Summary

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The benefits and risks of fluoroquinolones are favorable in the treatment of certain serious and life-threatening infectious diseases. However, the risk of serious AEs associated with fluoroquinolone use outweigh their benefits in less serious infectious diseases, such as in patients with ABS, ABECB, or uUTI when alternative treatment options are available. The FDA recommends that fluoroquinolones be used in patients with these conditions only if other treatment options are not available.

[19] Appropriate use of these antibiotics may help to preserve them for clinical use in patients with serious infections and in those without other options. Before any prescriptions for fluoroquinolones are written, healthcare providers must ask themselves these questions:

1. Does this patient really need to be treated with an antibiotic?
2. If this patient needs an antibiotic, is a fluoroquinolone the most appropriate option?