

# Antibiotic Commonsense

## Fluoroquinolones: Too Risky for Many Infections

By Brittany Schwandt, PharmD, BCPS

### Actions

- Do not prescribe quinolones when other antibiotics can be used. Only prescribe these agents when the benefit is certain and significant.
- If prescribed, select the most appropriate option and dose for the source.
- Let patients know that quinolones, while generally regarded as safe, have the rare potential to cause a variety of serious side effects.
- Instruct your patients to report any concerning symptoms immediately, including those listed in the medication handout.
- Be ready and willing to discontinue the quinolone at the first sign of any potentially serious reaction described in the product labeling.

### Background

Fluoroquinolones have become a mainstay of therapy for a wide range of conditions due to their ease of use, broad spectrum of activity and perceived safety. As of 2012, they accounted for nearly 1/3 of all outpatient prescriptions in the United States.<sup>1</sup> In 2014, retail pharmacies dispensed more than 31 million quinolones, with indications ranging from genitourinary to bronchitis and even viral respiratory conditions.<sup>2</sup>

Abundant overuse has revealed a dark side to these agents. In addition to a troubling rise in drug resistance—making the class no longer reliable as first-line empiric therapy for serious gram-negative infections—these agents are increasingly recognized to cause a range of devastating adverse events not often seen with other antimicrobial classes. Driven largely by patient advocacy groups, the United States Food and Drug Administration (FDA) announced its first major warning for the class in 2008 and followed with a series of concerning updates. (See figure 1.)

Figure 1. Summary of FDA warnings<sup>3,4</sup>

July 2008	Black box warning—tendinitis and tendon rupture.
August 2013	Peripheral neuropathy that can be severe or permanent.
May 2016	Avoid use for acute sinusitis, acute exacerbation of chronic bronchitis and cystitis.
July 2016	Black box warning—disabling and potentially permanent side effects of the tendons, muscles, joints, nerves and central nervous system.
July 2018	Mental health side effects. Severe blood sugar disturbances, including hypoglycemic coma.
December 2018	Aortic aneurysm and dissection—risk is double when taking fluoroquinolones vs. taking another or no antibiotic.

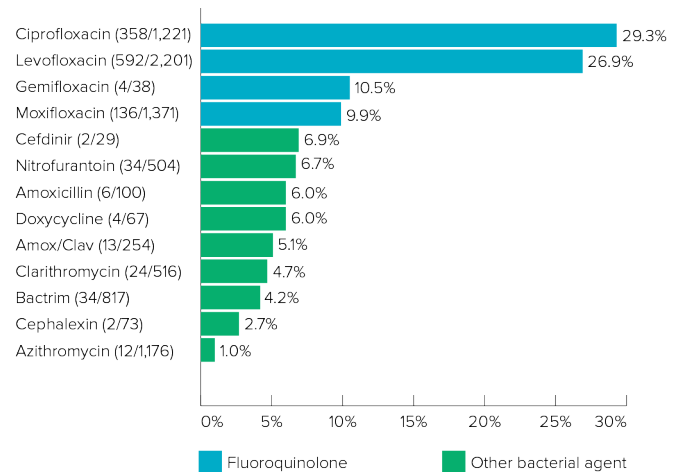
The FDA Antimicrobial Drugs Advisory Committee introduced fluoroquinolone-associated disability (FQAD) syndrome in 2015.<sup>5</sup> The syndrome includes previously healthy patients who develop disabling symptoms in at least 2 body systems lasting 30 days or more after stopping a quinolone. The symptoms can occur after a single dose, or weeks to months after stopping a course of therapy. FQAD includes a constellation of severe, disabling symptoms, including but not limited to:

- Tendon/joint/muscle dysfunction.
- Central nervous system effects—fatigue, insomnia, anxiety, headache, delirium, vertigo, dizziness, nightmares, depression.
- Peripheral nervous system impairment—neuropathy, numbness, tingling, burning, tremors.
- Sensory deficits—eye pain, vision impairment, tinnitus.
- Other symptoms—rash, sweating, hair loss, sensitive skin.

Patient reports to the FDA Adverse Events Reporting System 1997-2015 in which a quinolone was taken for cystitis, sinusitis or bronchitis, were screened for FQAD.<sup>5</sup> For comparison, the FDA reviewed submissions from patients who received alternative antibiotics for similar indications. Of more than 210,000 adverse events reported for quinolones, 1,122 described disabling symptoms. Of these, 178 met criteria for FQAD syndrome. Patients frequently reported their providers could not determine what caused their symptoms and were dismissive of patients who expressed concern for quinolone toxicity. Importantly, quinolones were associated with far more disabling side effects relative to alternative, first-line antibiotics. (See figure 2.)

Since surveillance depends on self-reporting, we don't know the true incidence of these adverse events. Estimates indicate 90-99% of adverse events aren't reported. Vague neurologic symptoms—like weakness, confusion and worsening anxiety or depression—may be incorrectly attributed to age or another etiology. They may then go unrecognized as an adverse reaction to a quinolone due to lack of awareness of the full spectrum of risk associated with these agents.<sup>6,7</sup>

**Figure 2. United States disability reports (%) among/serious outcome reports for sinusitis, bronchitis and UTI<sup>5</sup>**



## What can you do?

Avoid fluoroquinolones for patients with the following conditions or risk factors unless benefit clearly outweighs the risk.<sup>3,4,6,7,11,12</sup>

- Acute sinusitis, acute exacerbations of chronic obstructive pulmonary disease and cystitis unless no other option exists.
- Age 60 years or older.
- Pre-existing dementia, cognitive, neurologic or psychiatric conditions.
- Diabetes.
- Taking concomitant systemic corticosteroids, amiodarone, sotalol, procainamide or warfarin.
- Poorly controlled hypertension.
- Peripheral atherosclerotic vascular diseases.
- Heart, kidney or lung transplant.
- Pre-existing arrhythmia and/or baseline QTc > 440.
- History of *Clostridioides difficile* infection.
- Athletes.

Penicillin allergy is an oft-cited reason for receipt of a quinolone, yet for most patients this is not warranted. Many patients reporting an allergy have an unknown reaction or experienced the reaction as a child. When formally tested, however, 9 out of 10 do not have a true penicillin allergy.<sup>9</sup> For patients with penicillin reactions other than anaphylaxis or life-threatening cutaneous reactions, it is safe to use

a cephalosporin that does not share a similar side chain to a penicillin agent.<sup>10,11</sup> (See [www.ncbi.nlm.nih.gov/pmc/articles/PMC5681410/figure/F3](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC5681410/figure/F3).) For pneumonia or urinary tract infection, cefdinir is a suitable choice.

## What if you need to prescribe a quinolone?

Quinolones have a place in therapy for many conditions outside the scope of this article. When used for syndromes commonly encountered in the community setting, it's imperative to select the most appropriate agent for the suspected source and dose appropriately to minimize the risk for resistance. In general, when treating infections due primarily to gram-negative pathogens (i.e., urinary tract infection, intra-abdominal), select ciprofloxacin. Reserve levofloxacin and moxifloxacin for infections where gram-positive pathogens predominate (i.e., pneumonia).<sup>11</sup>

## Bottom Line

- Do not prescribe quinolones when other antibiotics can be used safely and effectively.
- If prescribed, select the most appropriate option and dose for the source.
- Counsel your patients to report any concerning symptoms, including those listed in the medication handout.

## References

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