

Stanford Antimicrobial Safety & Sustainability
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Think twice about that fluoroquinolone prescription

[Updated FDA boxed warning of serious side effects associated with fluoroquinolones](#)

On May 12, 2016, the Food and Drug Administration (FDA) issued a drug safety communication warning about potentially disabling side effects associated with the use of fluoroquinolone antibiotics and advising that their use be restricted. In particular, they advised that those side effects "...generally outweigh the benefits for patients with sinusitis, bronchitis, and uncomplicated urinary tract infections who have other treatment options" and that fluoroquinolones should not be used for those infections unless there are no alternative treatment options.

The FDA has previously repeatedly expressed concerns about the safety of this class of drugs (Table). These warnings were, however, deemed insufficient by an advisory panel that met in November 2015 and concluded that stronger statements were warranted [1]. Importantly, they further concluded that their analysis of the balance of benefits and risks of use of systemically administered fluoroquinolones leads to the conclusion that the current labeled indications for use in the treatment of acute bacterial sinusitis, acute exacerbations of chronic bronchitis or uncomplicated urinary tract infections are not warranted. This was not an equivocal recommendation – their votes were overwhelming.

Infectious Diseases Society of America guidelines recommend fluoroquinolones as an alternative to first line antibiotics (nitrofurantoin, fosfomycin, trimethoprim-sulfamethoxazole) for the treatment uncomplicated urinary tract infections. Antibiotic therapy is not recommended in acute bronchitis (which is almost always caused by viruses). Antibiotics do provide benefit for patients with moderate-to-severe (not mild) acute bacterial exacerbations of chronic bronchitis - but fluoroquinolones are considered only as an alternative to first-line therapy. Like acute bronchitis, acute sinusitis is overwhelmingly of viral, not bacterial, etiology. As a consequence, antibiotics are only recommended for selected patients with very severe disease, with "double-sickening" (improvement followed by worsening suggestive of bacterial superinfection), or non-improving symptoms for at least 10 days.

Thus, even prior to the FDA warning, fluoroquinolones (and other antibiotics) had no role in the management of patients with acute bronchitis, or in the overwhelming majority of patients with acute sinusitis, and they are not a first-line choice in patients with moderate-to-severe acute exacerbations of chronic bronchitis. They are also not among the first-line choices for treatment of uncomplicated urinary tract infection. Despite this, in 2014 in the U.S, at least 22.2 million individuals (32.8 million total prescriptions) were dispensed a prescription for a fluoroquinolone. There is obviously a disconnect between both the published data and authoritative recommendations and actual clinical practice. Perhaps this warning from the FDA will give us a reminder of the first rule of medical practice - "primum non nocere" - and force us to reconsider our (and our colleague's) uses of fluoroquinolones.

Table. Fluoroquinolone Safety Labeling*

- Boxed Warning
 - Tendinopathy and tendon rupture (Increased risks: age >60 years, concomitant corticosteroids, solid organ transplant)
 - Exacerbation of myasthenia gravis
- Warnings and Precautions Section
 - Hypersensitivity reactions
 - Hepatotoxicity
 - Central nervous system effects
(Altered mental status, seizures, tremors, psychosis, pseudotumor cerebri)
 - Peripheral neuropathy (potentially irreversible)
 - QT prolongation, Torsades de pointe
 - Blood glucose disturbance
 - Photosensitivity/phototoxicity

*Recent reports (not included in the labeling) have also suggested increased risks of retinal detachment and aortic aneurysm rupture.

References:

1. FDA Drug Safety Communication. <http://www.fda.gov/downloads/Drugs/DrugSafety/UCM500591.pdf>
2. 2015 Meeting Materials, Antimicrobial Drugs Advisory Committee (formerly known as the Anti-Infective Drugs Advisory Committee). November 5, 2015 Meeting of the Antimicrobial Drugs Advisory Committee. <http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/Anti-InfectiveDrugsAdvisoryCommittee/ucm424449.htm>