August 9, 2016

Subject: July 26, 2016 FDA updated Boxed Warnings and revisions to the Warnings and Precautions section for Fluoroquinolone antibiotics to include but not limited to:

Avelox (moxifloxacin)
Cipro (ciprofloxacin)
Cipro extended-release (ciprofloxacin extended-release)
Factive (gemifloxacin)
Levaquin (levofloxacin)
Moxifloxacin injection (moxifloxacin)
Ofloxacin (ofloxacin)

Dear Healthcare Provider:

The Quinolone Vigilance Foundation is committed to providing physicians and patients with the most current information available. In conjunction with the Food and Drug Administration to increase health care provider and patient awareness of both the risks and benefits of fluoroquinolones, we are sending this letter to share new information about fluoroquinolone antibiotics listed above.

The Black Box Warning and revisions to the Warnings and Precautions section of the fluoroquinolone labels have been updated effective July 26, 2016 to enhance warnings about their association with disabling and potentially permanent side effects and to limit their use in patients with less serious bacterial infections. The following changes and additions have been made to the labeling:

“Because the risk of these serious side effects generally outweighs the benefits for patients with acute bacterial sinusitis, acute exacerbation of chronic bronchitis and uncomplicated urinary tract infections, the FDA has determined that fluoroquinolones should be reserved for use in patients with these conditions who have no alternative treatment options[i],[ii],[iii] For some serious bacterial infections, including anthrax, sepsis, MRSA, and bacterial pneumonia among others, the benefits of fluoroquinolones outweigh the risks and it is appropriate for them to remain available as a therapeutic option[iv].”

While these fluoroquinolone antibiotics are effective in treating serious bacterial infections, an FDA safety review conducted on November 5, 2015 found that both oral and injectable fluoroquinolones are associated with disabling adverse reactions involving tendon ruptures[v], muscles, joints, nerve damage[vi] and the central, autonomic, and nervous systems. These adverse reactions can occur hours, weeks, months, and longer after exposure to fluoroquinolones and have the potentially to be permanent. In addition, fluoroquinolone antibiotics have been linked to neurodegenerative disorders, as per an FDA internal document dated April 17, 2013[vii].

Precautions statement on the label has been revised to read as follows: The labeling changes include an updated Boxed Warning and revisions to the Warnings and Precautions section of the label about the risk of disabling and potentially irreversible adverse reactions that can occur together. The label also contains new limitation-of-use statements to reserve fluoroquinolones for patients who do not have other available treatment options for acute bacterial sinusitis, acute bacterial exacerbation of chronic bronchitis and uncomplicated urinary tract infections. The patient Medication Guide that is required to be given to the patient with each fluoroquinolone prescription describes the safety issues associated with these medicines. [viii],[ix],[x]

Adverse Reactions section of the product insert has been revised for the following adverse events:

Fluoroquinolones have been associated with disabling and potentially irreversible serious adverse reactions that have occurred together including (please see prescribing instructions available at FDA.gov):

Box Warnings:

- Tendinitis and tendon rupture
- Peripheral neuropathy
- Central nervous system effects

Warnings:

- Anaphylactic reactions and allergic skin reactions, serious, occasionally fatal, may occur after first dose
- Hematologic (including agranulocytosis, thrombocytopenia), and renal toxicities may occur after multiple doses
- Hepatotoxicity: Severe, and sometimes fatal, hepatoxicity has been reported.
- Central nervous system effects, including convulsions, anxiety, confusion, depression, and insomnia may occur after the first dose.
- Clostridium difficile-associated colitis
- Prolongation of the QT interval and isolated cases of torsade de pointes have been reported.

Actions a health care provider should take in response to the new information:

Doctors should not prescribe fluoroquinolones for patients with acute bacterial sinusitis, acute exacerbation of chronic bronchitis, uncomplicated urinary tract infections or other common bacterial infections that can be treated with a safer alternative. Doctors should only prescribe to patients where no alternatives exist. Doctors and patients should discontinue the fluoroquinolone immediately and avoid the use of fluoroquinolones in patients who experience any of these serious adverse reactions. Adverse reactions can be reported to the FDA MedWatch system at FDA.gov.

It is our hope that this information will facilitate and increase the safe and vigilant use of fluoroquinolone antibiotics by your patients . Please share this letter with associates in your practice.

Thank you for taking time out of your busy schedule to read this letter.

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i http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/Anti-InfectiveDrugsAdvisoryCommittee/UCM477657.pdf
ii http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/Anti-InfectiveDrugsAdvisoryCommittee/UCM470453.pdf
iii http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm513183.htm
iv http://www.fda.gov/AdvisoryCommittees/Calendar/ucm465275.htm
v http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm126085.htm
vi http://www.fda.gov/Drugs/DrugSafety/ucm365050.htm
vii http://www.saferpills.org/wp-content/uploads/2014/10/FOI_130417-ODS-Postmarketing-Safety-Review-1.pdf
viii http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/Anti-InfectiveDrugsAdvisoryCommittee/UCM477657.pdf
ix http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/Anti-InfectiveDrugsAdvisoryCommittee/UCM470453.pdf
x http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm513183.htm