



27 MAY 2019

**FDA ADVISORY**  
No. **2019-128**

**TO: ALL HEALTHCARE PROFESSIONALS AND MARKET AUTHORIZATION HOLDERS**

**SUBJECT: Safety Information: Fluoroquinolones and risk of aortic aneurysm and dissection**

### **Introduction**

The US FDA searched their adverse event reporting system database and reviewed epidemiological studies to investigate the association between fluoroquinolone antibacterial use and the risk of aortic aneurysm and dissection. The review found that fluoroquinolone antibiotics can increase the occurrence of rare but serious events of ruptures or tears in the main artery of the body, called the aorta. These tears, called aortic dissections, or ruptures of an aortic aneurysm can lead to dangerous bleeding or even death.

### **Scientific Discussion**

Fluoroquinolones are broad-spectrum antibacterial agents. It exhibits bactericidal activity by interfering with bacterial DNA replication, specifically by inhibiting DNA gyrase or topoisomerase.

In the Philippines, there are eight systemic fluoroquinolones registered as prescription-only medicines, these include:

- |                 |                 |
|-----------------|-----------------|
| • Ciprofloxacin | • Norfloxacin   |
| • Enrofloxacin  | • Ofloxacin     |
| • Levofloxacin  | • Pefloxacin    |
| • Moxifloxacin  | • Prulifloxacin |

Fluoroquinolones are indicated for the treatment of certain bacterial infections. Resistance to these agents should be considered before commencing therapy.

Fluoroquinolones have been associated with collagen degradation, raising safety concerns related to more serious collagen disorders with use of these antibiotics including aortic aneurysm and dissection. Collagen is a major extracellular matrix component of the aortic wall. As fluoroquinolones may induce degradation of collagen causing tendinopathy, it may cause or aggravate aortic aneurysm and dissection by a similar mechanism.

To date, FDA has not received any adverse drug reactions reports of aortic aneurysm or dissection with fluoroquinolones.




### **Safety Advisory**

Healthcare professionals are advised to avoid prescribing fluoroquinolones to patients who have aortic aneurysm or at risk for an aortic aneurysm, such as patients with peripheral atherosclerotic vascular disease, hypertension, certain genetic conditions such as Marfan syndrome and Ehlers-Danlos syndrome, and elderly patients. The benefit of using fluoroquinolones to these patients should be assessed by the prescribers prior to initiation of therapy. It should be prescribed to these patients only when no other treatment options are available.

Advise all patients to seek immediate medical treatment for any symptoms associated with aortic aneurysm and stop the fluoroquinolone therapy immediately if suggestive of aortic aneurysm or dissection.

### **Information for Market Authorization Holders**

The Market Authorization Holders of systemic fluoroquinolones containing active pharmaceutical ingredients as listed above shall update their respective package inserts to appear the information on risk of aortic aneurysm and dissection on the use of systemic fluoroquinolone antibiotics. This information shall be discussed under Warnings and Precautions. MAHs shall submit a variation application within 3 months after this issuance.

  
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