

9 June 2020

Direct Healthcare Professional Communication on the risk of risk of aortic aneurysm and dissection associated with the Systemic and inhaled fluoroquinolones:

Dear Healthcare Professional,

We Alpha Pharma Industries, Saudi Arabia holder of the fluoroquinolones antibiotic **Eradocin (Levofloxacin) 500mg & 750 mg Film Coated Tablets**, and in compliance with the Saudi food and drug Authority (SFDA) would like to inform you of the following.

Summary

- Systemic and inhaled fluoroquinolones may increase the risk of aortic aneurysm and dissection, particularly in older people.
- In patients at risk for aortic aneurysm and dissection, fluoroquinolones should only be used after careful benefit-risk assessment and after consideration of other therapeutic options.
- Conditions predisposing to aortic aneurysm and dissection include a family history of aneurysm disease, pre-existing aortic aneurysm or aortic dissection, Marfan syndrome, vascular Ehlers-Danlos syndrome, Takayasu arteritis, giant cell arteritis, Behcet ' s disease, hypertension, and atherosclerosis.
- Patients should be advised about the risk of aortic aneurysm and dissection and told to seek immediate medical attention in the emergency department in case of sudden severe abdominal, chest or back pain.

Background on the safety concern

Fluoroquinolones are antibiotics approved for the treatment of several bacterial infections, including life-threatening ones. fluoroquinolone antibiotics include ciprofloxacin, moxifloxacin, levofloxacin, ofloxacin and norfloxacin

Data from epidemiologic and non-clinical studies indicate an increased risk of aortic aneurysm and dissection after treatment with fluoroquinolones.

The epidemiological studies [1-3] report an about 2-fold increase in the risk of aortic aneurysm and dissection in patients taking systemic fluoroquinolones compared with patients taking no antibiotics or other antibiotics (amoxicillin); with older people being at higher risk.

A non-clinical study [4] reported that ciprofloxacin increases the susceptibility to aortic dissection and rupture in a mouse model. This finding is likely a class effect similar to fluoroquinolones being harmful to tendon tissue and thereby increasing the risk of tendon disorders



Aortic aneurysm and dissection are rare events, occurring with an incidence of about 3-30 of 100,000 persons per year. Factors that increase the risk include family history of aneurysm disease, pre-existing aortic aneurysm or aortic dissection, Marfan syndrome, vascular Ehlers Danlos syndrome, Takayasu arteritis, giant cell arteritis, Behcet ' s disease, hypertension, and atherosclerosis.

Therefore, systemic or inhaled fluoroquinolones should only be used after careful benefit-risk assessment and after consideration of other therapeutic options in patients at risk for aortic aneurysm and dissection.

Patients should be advised about this risk and told to seek immediate medical attention in case of sudden abdominal, chest or back pain.

Call for Reporting:

The treating healthcare physicians are advised to report the adverse events in accordance with the national spontaneous reporting system.

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Should you have any questions, please do not hesitate to contact us. We will keep you informed as further information becomes available.

Yours faithfully,
Suhail Ahmad Khalaf
Acting QPPV

References:

[1] Daneman N, Lu H, Redelmeier DA. Fluoroquinolones and collagen associated severe adverse events: a longitudinal cohort study. *BMJ Open*. 2015 Nov 18;5(11):e010077

[2] Lee CC, Lee MT, Chen YS, Lee SH, Chen YS, Chen SC, Chang SC. Risk of Aortic Dissection and Aortic Aneurysm in Patients Taking Oral Fluoroquinolone. *JAMA Intern Med*. 2015 Nov;175(11):1839-47.

[3] Pasternak B, Inghammar Mand Svanstrom H. Fluoroquinolone use and risk of aortic aneurysm and dissection: nationwide cohort study. *BMJ* 2018; 360: k678.

[4] LeMaire SA, Zhang L, Luo W, Ren P, Azares AR, Wang Y, Zhang C, Coselli JS, Shen YH. Effect of Ciprofloxacin on Susceptibility to Aortic Dissection and Rupture in Mice. *JAMA Surg*. 2018 Jul 25:e1 81804. [Epub ahead of print]