November 2018

Direct Healthcare Professional Communication

Systemic and inhaled fluoroquinolones: risk of aortic aneurysm and dissection

Dear

Following a European safety review, Marketing Authorisation Holders of medicines containing fluoroquinolones for systemic and inhalation use, in agreement with the Medicines and Healthcare Products Regulatory Agency (MHRA), would like to inform you of the following new safety information:

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, Behçet'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 in Europe for the treatment of several bacterial infections, including life-threatening ones. Examples of fluoroquinolone antibiotics include ciprofloxacin, moxifloxacin and levofloxacin.

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, Behçet'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

Suspected adverse reactions should be reported to the MHRA through the Yellow Card Scheme. When reporting, please provide as much information as possible. It is easiest and quickest to report ADRs online via the Yellow Card website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Alternatively, prepaid Yellow Cards for reporting are available by writing to FREEPOST YELLOW CARD (no other address details necessary), by emailing yellowcard@mhra.gov.uk, at the back of the British National Formulary (BNF), by telephoning the Commission on Human Medicines (CHM) free phone line: 0800-731-6789, or by downloading and printing a form from the Yellow Card section of the MHRA website.

Yours sincerely,

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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 M and Svanström 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:e181804. [Epub ahead of print]

Company contact details

These materials are being sent to you on behalf of the group of companies listed below, who are Marketing Authorisation holders for medicines containing fluoroquinolones for systemic or inhalation use. If you require additional information, please contact the medical information services of the individual company.

Company	**Medical Information contact details**
Accord – UK Ltd (distributor of Actavis Group PTC ehf) Accord Healthcare Limited	Email: medinfo@accord-healthcare.com Telephone: 01271 385 257
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Claris Lifesciences UK Limited	Email: medinfo@peckforton.com Telephone: 01628 771 800
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