

Direct Healthcare Professional Communication

29.10. 2020

Systemic and inhaled fluoroquinolones: risk of heart valve regurgitation/incompetence

Dear Healthcare professional,

Marketing authorisation holders of fluoroquinolone antibiotics products in agreement with the European Medicines Agency and the Federal Institute for Drugs and Medical Devices would like to inform you of the risk of heart valve regurgitation/incompetence associated with fluoroquinolones for systemic and inhalation use.

Summary

- *Systemic and inhaled fluoroquinolones may increase the risk of heart valve regurgitation/incompetence.*
- *Conditions predisposing to heart valve regurgitation/incompetence include congenital or pre-existing heart valve disease, connective tissue disorders (for example Marfan syndrome or Ehlers-Danlos syndrome), Turner syndrome, Behçet's disease, hypertension, rheumatoid arthritis, and infective endocarditis.*
- *In patients at risk for heart valve regurgitation/incompetence, systemic and inhaled fluoroquinolones should only be used after careful benefit-risk assessment and after consideration of other therapeutic options.*
- *Patients should be advised to seek immediate medical attention in case of acute dyspnoea, new onset of heart palpitations, or development of oedema of the abdomen or lower extremities.*

Background on the safety concern

Fluoroquinolones are antibiotics approved in the European Union for the treatment of certain bacterial infections, including life-threatening ones. Because they can have serious and long-lasting side effects, their use is generally restricted to infections where it is considered inappropriate to use other antibiotics commonly recommended for these infections (risk subject to a Direct Healthcare Professional Communication circulation in March/April 2019, link to national website if applicable). Fluoroquinolones should only be used after carefully assessing its likely benefits and its risks including that of aortic aneurysm and dissection (risk subject to a Direct Healthcare Professional Communication circulation in October 2018, link to national website if applicable).

A recent epidemiological study [1] reported an about 2-fold increase in risk of mitral and aortic regurgitation in patients taking systemic fluoroquinolones compared with patients taking other antibiotics (amoxicillin or azithromycin).

Several medically confirmed cases of heart valve regurgitation/incompetence affecting any heart valve have been reported in patients receiving fluoroquinolones with probable or possible causal association. These data indicate that fluoroquinolones can cause heart valve regurgitation/incompetence.

Additionally, a laboratory study [2] reported that exposure to ciprofloxacin led to collagen degradation in aortic myofibroblasts cells donated from patients with aortopathy, including aortic regurgitation. This finding provides insight into how fluoroquinolone-associated degradation of connective tissue may be associated with heart valve regurgitation/incompetence. Collagen degradation has also been postulated for fluoroquinolone-associated disorders of tendons and the aorta.

Factors that increase the risk for heart valve regurgitation/incompetence include congenital or pre-existing heart valve disease, connective tissue disorders (for example Marfan syndrome or Ehlers-Danlos syndrome), Turner syndrome, Behçet's disease, hypertension, rheumatoid arthritis, and infective endocarditis.

In patients at risk for heart valve regurgitation/incompetence, systemic and inhaled fluoroquinolones should only be used after careful benefit-risk assessment and after consideration of other therapeutic treatment options.

Patients should be advised to seek immediate medical attention in case of acute dyspnoea, new onset of heart palpitations, or development of oedema of the abdomen or lower extremities.

Call for reporting

Reporting suspected adverse reactions is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

Company contact point

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References

- [1] Etminan M, Sodhi M, Ganjizadeh-Zavareh S, Carleton B, Kezouh A, Brophy JM. Oral Fluoroquinolones and Risk of Mitral and Aortic Regurgitation. *J Am Coll Cardiol*. 2019 Sep 17;74(11):1444-1450.
- [2] Guzzardi DG, Teng G, Kang S, Geeraert PJ, Pattar SS, Svystonyuk DA, Belke DD, Fedak PWM. Induction of human aortic myofibroblast-mediated extracellular matrix dysregulation: A potential mechanism of fluoroquinolone-associated aortopathy. *J Thorac Cardiovasc Surg*. 2019 Jan;157(1):109-119.