BRITISH GENERIC MANUFACTURERS ASSOCIATION

December 2020

# Important safety information

## Direct Healthcare Professional Communication

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

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 heart valve regurgitation/incompetence.
- Conditions predisposing to heart valve regurgitation/incompetence include congenital or pre-existing heart valve disease, hypertension, connective tissue disorders (for example Marfan syndrome or Ehlers-Danlos syndrome), Turner syndrome, Behçet's disease, 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 about the risk of heart valve regurgitation/incompetence and told to seek immediate medical attention at a hospital accident and emergency department 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 for the treatment of certain bacterial infections, including life-threatening ones. Examples of fluoroquinolone antibiotics include ciprofloxacin, moxifloxacin and levofloxacin.

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. This risk was communicated in Drug Safety Update March 2019; https://www.gov.uk/drug-safety-update

Fluoroquinolones should only be used after carefully assessing its likely benefits and its risks including that of heart valve regurgitation/incompetence. This risk was communicated in Drug Safety Update November 2018.

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, hypertension, connective tissue disorders (for example Marfan syndrome or Ehlers-Danlos syndrome), Turner syndrome, Behçet's disease, rheumatoid arthritis, and infective endocarditis.

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

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.

**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.

**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 and inhalation use. If you require additional information, please contact the medical information services of the individual company.

## Reporting of side effects

Please report suspected adverse drug reactions (ADRs) to the MHRA through the Yellow Card scheme.

You can report via:

- the Yellow Card website www.mhra.gov.uk/yellowcard
- the free Yellow Card app available from the Apple App Store or Google Play Store
- some clinical IT systems (EMIS/SystmOne/Vision/MiDatabank) for healthcare professionals

Alternatively, you can report a suspected side effect to the Yellow Card scheme by calling 0800 731 6789 for free, Monday to Friday between 9am and 5pm. You can leave a message outside of these hours.

When reporting please provide as much information as possible. By reporting side effects, you can help provide more information on the safety of this medicine.

Yours sincerely,

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