

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,



Paul Fleming

Technical Director

Tel: +44 (0)20 7457 2841

Mobile: +44 (0)7774 775150



65 Gresham Street, London, EC2V 7NQ, UK
www.britishgenerics.co.uk

Company	Medical Information contact details
Accord-UK Ltd and Accord Healthcare Limited	medinfo@accord-healthcare.com Telephone: 01271 385 257 https://www.medicines.org.uk/emc/company/1603 https://www.medicines.org.uk/emc/company/3203
Advanz Pharma	medicalinformation@advanzpharma.com Telephone: 08700 70 30 33 https://www.medicines.org.uk/emc/company/2507
Baxter Healthcare Ltd	medinfo_uki@baxter.com Telephone: 01635 206345 https://www.medicines.org.uk/emc/company/65
Bayer plc	medical.information@bayer.co.uk Telephone: 0118 206 3116 https://www.medicines.org.uk/emc/company/13
Bowmed Ibisqus Limited and partner companies	medinfo@bowmed.com Telephone: 01483 212 151 https://www.medicines.org.uk/emc/company/3210
Bristol Laboratories Limited	info@bristol-labs.co.uk Telephone: 01442 200 922 https://www.medicines.org.uk/emc/company/2944
Brown & Burk (UK) Ltd	pv@bbukltd.com and pvsupport@microlabs.in Telephone: 0203 384 7188 https://www.medicines.org.uk/emc/company/4017
Fresenius Kabi Limited	Medical.Information-UK@fresenius-kabi.com Telephone: 01928 533 575 https://www.medicines.org.uk/emc/company/2745
Hikma Farmacêutica (Portugal), S.A.	portugaleuparmacovigilance@hikma.com Telephone: 00 351 210 438 540
Infomed Fluids S.r.L	info@infomedfluids.com Telephone: 00 40 21 345 02 22
Ipca Laboratories UK Ltd	ipca@callisto-consulting.co.uk Telephone: 01332 959 126 https://www.medicines.org.uk/emc/company/4122
Kent-Athlone Pharma Group Beacon Pharmaceuticals Limited	Medical@Kent-athlone.com Telephone: 01233 506 574 https://www.medicines.org.uk/emc/company/2550
Medreich PLC	info@medreich.co.uk Telephone: 0208 831 1580, out of hours 07590 831 289

Company	Medical Information contact details
A. Menarini Farmaceutica Internazionale S.r.l.	menarini@medifformation.co.uk Telephone: 0800 085 8678 https://www.medicines.org.uk/emc/company/644
Milpharm Limited	MEDINFO@aurobindo.com Telephone: 0208 845 8811 https://www.medicines.org.uk/emc/company/3006
Mylan UK Healthcare Ltd (a Viatris company)	info.uk@viatris.com Telephone: 0170 785 3000 https://www.medicines.org.uk/emc/company/3338
Noridem Enterprises Ltd	pv@demo.gr Telephone: 00 30 2108 161 802
Pfizer UK	www.pfizermedicalinformation.co.uk Telephone: 01304 616 161 https://www.medicines.org.uk/emc/company/105
Ranbaxy UK Limited, a SUN PHARMA company	medinfoeurope@sunpharma.com Telephone: 0208 848 5052 https://www.medicines.org.uk/emc/company/2272
Rivopharm UK Ltd	pv.sanoswiss@biomapas.com Telephone: 02034 328 085 https://www.medicines.org.uk/emc/company/3287
Sandoz Limited	Sandozgb@EU.propharmagroup.com Telephone: 01276 698 101 https://www.medicines.org.uk/emc/company/2502
Strides Pharma UK Ltd	dl-drugsafety@strides.com Telephone: 08708 510 270 https://www.medicines.org.uk/emc/company/3314
Teva UK Limited	medinfo@tevauk.com Telephone: 0207 540 7117 https://www.medicines.org.uk/emc/company/3027
Tillomed Laboratories	medical.information@tillomed.co.uk Telephone: 01480 402 400 https://www.medicines.org.uk/emc/company/4082
Torrent Pharma (UK) Ltd.	Medinfo.torrent@apcerls.com Telephone: 0800 088 5366
Wockhardt UK Ltd	Drug.Safety@wockhardt.co.uk Telephone: 01978 661 261 https://www.medicines.org.uk/emc/company/35