July 2023

Direct Healthcare Professional Communication

Systemic and inhaled fluoroquinolone antibiotics – reminder on restrictions of use

Active Substances:

Ciprofloxacin
Delafloxacin
Levofloxacin
Moxifloxacin
Ofloxacin

For systemic and inhalation route

Direct Healthcare Professional Communication

Systemic and inhaled fluoroquinolone antibiotics – reminder on restrictions of use

Dear Healthcare Professional,

Marketing Authorisation Holders of fluoroquinolone antibiotics, in agreement with the Medicines and Healthcare products Regulatory Agency (MHRA) and the European Medicines Agency (EMA), would like to remind you of the following:

Summary

- Recent study data suggest that fluoroquinolones (ciprofloxacin, delafloxacin, levofloxacin, moxifloxacin, ofloxacin) continue to be prescribed outside of the authorised uses.
- Systemic and inhaled fluoroquinolones should **NOT** be prescribed for:
    - patients who have previously had serious adverse reactions with a quinolone or fluoroquinolone antibiotic;
    - non-severe or self-limiting infections (such as pharyngitis, tonsillitis and acute bronchitis);
    - some mild to moderate infections (such as in acute exacerbation of chronic bronchitis, chronic obstructive pulmonary disease, or uncomplicated cystitis) unless

other antibiotics that are commonly recommended for these infections are considered inappropriate;
    - non-bacterial infections, e.g. non-bacterial (chronic) prostatitis;
    - preventing travellers' diarrhoea or recurrent lower urinary tract infections.
- Systemic and inhaled fluoroquinolones are associated with a risk of serious, disabling, long-lasting and potentially irreversible adverse reactions. These products should be prescribed only for authorised indications and after careful assessment of the benefits and risks in the individual patient.
- The MHRA has reviewed these recent study data, alongside data from other sources. It will prepare communications for UK healthcare professionals about any additional regulatory actions in the UK as a result of this review. These will be shared in the coming months.

Background to safety concern

The European Medicines Agency (EMA) introduced recommendations to restrict the use of systemic and inhaled fluoroquinolones following an EU-wide review conducted in 2018 to evaluate the risk of serious and long-lasting (lasting months or years), disabling, and potentially irreversible adverse reactions, sometimes affecting multiple systems, organ classes, and senses. As a consequence of the review conducted by EMA, the use of fluoroquinolone medicines was restricted in 2019.

These serious adverse reactions can include tendinitis, tendon rupture, arthralgia, pain in extremities, gait disturbance, neuropathies associated with paraesthesia, depression, fatigue, memory impairment, hallucinations, psychosis, sleep disorders and impaired senses (hearing, vision, taste and smell). Tendon damage (especially to Achilles tendon but other tendons can also be involved) can occur within 48 hours of commencing treatment or the effects can be delayed for several months and become apparent after stopping treatment.

An EMA-funded study was carried out ("Impact of European Union Label Changes for Fluoroquinolone Containing Medicinal Products for Systemic and Inhalation Use" (EUPAS37856)), which was based on an analysis of prescribing rates for fluoroquinolones in six European healthcare databases (from Belgium, France, Germany, the Netherlands, Spain and the United Kingdom).

The study suggests that fluoroquinolones have been used outside the authorised indications. However, due to the limitations of the study no definitive conclusions can be drawn.

- **Healthcare professionals** are reminded to advise patients:
    - of the risk of these serious adverse reactions;
    - of the potential long-lasting and serious nature of these effects;
    - to stop treatment at the first signs of a serious adverse reaction, such as tendinitis or tendon rupture, muscle pain, muscle weakness, joint pain, joint swelling, peripheral neuropathy, and central nervous system effects, and to contact their doctor immediately for further advice.

- **Special caution** should be taken in patients who concurrently are treated with corticosteroids, in people older than 60 years, patients with renal impairment, and patients who have undergone solid organ transplants, as the risk of fluoroquinolone-induced tendinitis and tendon rupture may be exacerbated in these patients.

Further information

For more details, please refer to the EMA communication at:
https://www.ema.europa.eu/en/news/fluoroquinolone-antibiotics-reminder-measures-reduce-risk-long-lasting-disabling-potentially

Call for reporting

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

- the Yellow Card website https://yellowcard.mhra.gov.uk/
- 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. When reporting please provide as much information as possible, including information about medical history, any concomitant medication, timing onset, treatment dates, and product brand name. Adverse events can also be reported to the MAH via the contact details below.

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. Where you are a lead practitioner, please share the information with colleagues in your practice. If you require additional information, please contact the medical information services of the individual company.

Mark Samuels
Chief Executive Officer
info@britishgenerics.co.uk

BRITISH GENERIC MANUFACTURERS ASSOCIATION

Company contact point

Table include:

<A table of Marketing authorisation holders and contact points>

MA Holder	Contact Email	SmPC/RMM location	Contact Med Info Phone Number
Milpharm	MEDINFO@aurobindo.com	https://www.medicines.org.uk/emc/company/3006	+44 (0) 208 845 8811
Viatris	pv.uk@viatris.com	Ofloxacin **200mg**: https://www.medicines.org.uk/emc/product/8481/smpc Ofloxacin **400mg**: https://www.medicines.org.uk/emc/product/8480/smpc	+44 (0) 800 121 8267
Noridem Enterprises Limited	medical@kent-athlone.com	https://medicines.kentpharma.co.uk	+44 (0) 123 350 6574
Bayer	medical.information@bayer.co.uk	Ciproxin: https://www.medicines.org.uk/emc/product/885 Avelox: https://www.medicines.org.uk/emc/product/6771	+44 (0) 118 206 3116
Wockhardt	Drug.Safety@wockhardt.co.uk		+44 (0) 1978 661 261
Chiesi	medinfo.uk@chiesi.com	eMC UK: https://www.medicines.org.uk/emc/product/7202/smpc eMC NI: https://www.emcmedicines.com/en-gb/northernireland/medicine?id=290b2d0a-db37-40cd-96fb-36ddaad86fc7&type=smpc	+44 (0) 1748 827 271
Tilomed	Medical.Information@Tillomed.co.uk	https://www.medicines.org.uk/emc/product/11584	+44 (0) 1480 402 400
Teva UK Limited	medinfo@tevauk.com	https://products.tevauk.com/healthcare-professionals/medicine-range	+44 (0)207 540 7117
Mercury Pharmaceuticals Ltd	medicalinformation@advanzpharma.com	https://www.medicines.org.uk/emc/company/2507	+44 (0) 208 588 9131
Fresenius Kabi	Medical.information-UK@fresenius-kabi.com	https://www.medicines.org.uk/emc/company/2745	+ 44 (0) 1928 533 575
Brown and Burk (UK) Ltd	pv@bbukltd.com	https://www.medicines.org.uk/emc/company/4017	+ 44(0)203 384 7188
Hikma Farmacêutica (Portugal), S.A.	portugaleupharmacvigilance@hikma.com	https://www.consilienthealth.co.uk/products/	+351 210 438 540
Kent Pharma UK Limited	medical@kent-athlone.com	https://medicines.kentpharma.co.uk	+44 (0) 123 350 6574