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Direct Healthcare Professional Communication

Fluoroquinolone antibiotics – risk of disabling, long-lasting and potentially irreversible side effects

New restrictions on prescribing for ciprofloxacin, levofloxacin, moxifloxacin, and ofloxacin for safety reasons

Dear Professor Scott,

Following a European safety review, Marketing Authorisation Holders of medicines containing quinolone and fluoroquinolone antibiotics, in agreement with the MHRA and the European Medicines Agency (EMA), would like to inform you of the following new safety information:

Summary

- **Disabling, long-lasting, and potentially irreversible adverse reactions mainly affecting musculoskeletal and nervous systems, have been reported with quinolone and fluoroquinolone antibiotics.**
- **As a consequence, the benefits and risks of all quinolone and fluoroquinolone antibiotics and their indications across the EU have been reviewed.**
- **Do not prescribe any quinolone and fluoroquinolone antibiotic for:**
    - **non-severe or self-limiting infections, or non-bacterial conditions**
    - **particular types of mild to moderate infections* unless other antibiotics that are commonly recommended for these infections are considered inappropriate (such as acute exacerbation of chronic bronchitis and chronic obstructive pulmonary disease (COPD))**
- **avoid use in patients who have previously had serious adverse reactions with a quinolone or fluoroquinolone antibiotic.**

- **Ciprofloxacin or levofloxacin should no longer be prescribed for uncomplicated cystitis unless other antibiotics that are commonly recommended are considered inappropriate.**
- **Exercise special caution when prescribing these medicines for the elderly, patients with renal impairment, patients with solid organ transplants, and patients concurrently treated with corticosteroids, since the risk of fluoroquinolone-induced tendinitis and tendon rupture may be exacerbated in these patients. Concomitant use of corticosteroids with fluoroquinolones should be avoided.**
- **Advise patients to stop treatment at the first signs of a serious adverse reaction, such as tendinitis and tendon rupture, muscle pain, muscle weakness, joint pain, joint swelling, peripheral neuropathy and central nervous system effects and to contact their doctor for further advice.**
- **Medicinal products containing nalidixic acid will be removed from the market.**

***Please refer to the product-specific Summary of Product Characteristics for ciprofloxacin, levofloxacin, moxifloxacin and ofloxacin for the full updated indications and precautions/warnings.**

Background on the safety concern

EMA has reviewed systemic and inhaled quinolone and fluoroquinolone antibiotics to evaluate the risk of serious, long-lasting (lasting months or years), disabling and potentially irreversible adverse reactions that mainly affect the musculoskeletal and nervous systems.

Serious adverse reactions of the musculoskeletal system include tendinitis, tendon rupture, myalgia, muscle weakness, arthralgia, joint swelling and gait disturbance.

Serious peripheral and central nervous system effects include peripheral neuropathy, insomnia, depression, fatigue, memory impairment, as well as impairment of vision, hearing, smell and taste.

Only a few cases of these disabling and potentially irreversible adverse reactions have been reported, but under-reporting can be assumed. Due to the seriousness of these reactions in previously healthy people, any decision to prescribe quinolones and fluoroquinolones should be taken after a careful assessment of the benefits and risk in each case.

The product information for all fluoroquinolone-containing medicines will be updated with this new information.

Fluoroquinolone medicines available in UK

- Ciprofloxacin
- Levofloxacin
- Moxifloxacin
- Ofloxacin

(The product information of fluoroquinolones has been also recently updated to include the risk of aortic aneurysm and dissection. See relevant information on https://www.gov.uk/drug-safety-update/systemic-and-inhaled-fluoroquinolones-small-increased-risk-of-aortic-aneurysm-and-dissection-advice-for-prescribing-in-high-risk-patients)

Further information

For more details, please refer to EMA review at [https://www.ema.europa.eu/en/medicines/human/referrals/quinolone-fluoroquinolone-containing-medicinal-products] and to the updated product information at http://www.mhra.gov.uk/spc-pil/

Call for reporting

Healthcare professionals should report suspected adverse drug reactions (ADRs) in patients taking quinolone or fluoroquinolone antibiotics using the Yellow Card website or via the Yellow Card app. When reporting please provide as much information as possible.

Download the app today via iTunes Yellow Card for iOS devices or via PlayStore Yellow Card for Android devices.

Alternatively, report ADRs via the Yellow Card website - https://yellowcard.mhra.gov.uk/ or on prepaid Yellow Cards 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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BRITISH GENERIC MANUFACTURERS ASSOCIATION

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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.

Company	**Medical Information contact details**
Accord – UK Ltd / Accord Healthcare Limited	Email: medinfo@accord-healthcare.com Telephone: 01271 385 257
AFDOS Pharmaceuticals Limited	Email: medinfo@afdospharma.com Telephone: 01582 809 833
Alkaloid-Int d.o.o	Email: Pharmacovigilance@alkaloid.si Telephone: 00 386 1 3004 293
Bayer plc	Email: medical.information@bayer.co.uk Telephone: 0118 206 3116
Bowmed Ibisqus Ltd and partner MAHs	Email: medinfo@bowmed.com Telephone: 01483 212 151
Britannia Pharmaceuticals Ltd	Email: enquiries@medinformation.co.uk Telephone: 01483 920 763
Brown and Burk (UK) Ltd	Email: pv@bbukltd.com and pvsupport@microlabs.in Telephone: 0203 384 7188
Claris Lifesciences UK Limited	Email: medinfo@peckforton.com Telephone: 01628 771 800
DCC Vital (Beacon Pharmaceuticals)	Email: medical@dccvital.com Telephone: 01233 506 574 or 00 353 86 839 4447
Dr Reddy's Laboratories (UK) Ltd	Email: DrReddys@professionalinformation.co.uk Telephone: 01748 828 873
Fresenius Kabi Limited	Email: Medical.Information-UK@fresenius-kabi.com Telephone: 01928 533 575

Generics (UK) Ltd t/a Mylan	Email: info.uk@mylan.co.uk Telephone: 01748 828 888
Hikma Farmaceutica (Portugal), S.A	Email: portugaleupharmacovigilance@hikma.com Telephone: 00 351 210 438 540
Infomed Fluids SRL	Email: office@infomedfluids.ro Telephone: 00 40 21 345 02 22
Medreich PLC	Email: info@medreich.co.uk Telephone: 0208 831 1580
Milpharm Ltd	Email: medinfo@aurobindo.com Telephone: 0208 845 8811
Noridem Enterprises Ltd.	Email: pv@demo.gr Telephone: 00 30 210 8161 802
Pfizer UK	Email: Medical.Information@pfizer.com Telephone: 01304 616 161
Ranbaxy UK Limited a Sun Pharma company	Email: medinfoeurope@sunpharma.com Telephone: 0208 848 8688
Sandoz Limited	Email: sandoz@professionalinformation.co.uk Telephone: 01276 698 101
Sanofi	Email: uk-medicalinformation@sanofi.com Telephone: 0845 372 7101
Teva and Teva Group entities	Email: medinfo@tevauk.com Telephone: 0207 540 7117
Tillomed Laboratories Ltd	Email: medinfo@tillomed.co.uk Telephone: 01480 402 400
Torrent Pharma (UK) Ltd	Email: Drugsafety@torrentpharma.co.uk Telephone: 01293 574 180
Wockhardt UK Limited	Email: drug.safety@wockhardt.co.uk Telephone: 01978 669 272