PLEASE READ

IMPORTANT MEDICINE SAFETY INFORMATION

APPROVED BY THE HPRA

An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Direct Healthcare Professional Communication

8th June 2023

Systemic and inhaled fluoroquinolone antibiotics – reminder on restrictions of use

Ciprofloxacin; Delafloxacin; Levofloxacin; Moxifloxacin

Dear Healthcare Professional,

Marketing authorisation holders of fluoroquinolone antibiotics in agreement with the European Medicines Agency (EMA) and the Health Products Regulatory Authority, would like to remind you of the following:

Summary

- Recent study data suggest that fluoroquinolones continue to be prescribed outside of the recommended 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);
    - mild to moderate infections (including uncomplicated cystitis, acute exacerbation of chronic bronchitis and chronic obstructive pulmonary disease (COPD), acute bacterial rhinosinusitis and acute otitis media) 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 very rare, serious, disabling, long-lasting and potentially irreversible adverse reactions. These products should be prescribed only for approved indications and after careful assessment of the benefits and risks in the individual patient.

Background to safety concern

The EMA made strong 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 mainly affecting the musculoskeletal and nervous system. As a consequence of the review conducted by EMA, the use of fluoroquinolone medicines was significantly 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 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 may still be 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 immediately seek a physician at the first signs of these serious adverse reactions prior to continuing treatment

- **Special caution** should be taken in patients who concurrently are treated with corticosteroids, in elderly, 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

https://www.ema.europa.eu/en/news/fluoroquinolone-antibiotics-reminder-measures-reduce-risk-long-lasting-disabling-potentially.

Call for reporting

Reporting suspected adverse reactions after authorisation of the medicinal product 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 HPRA Pharmacovigilance Website: www.hpra.ie.

Company contact point

Suspected adverse reactions should also be reported to the relevant Marketing Authorisation Holders (see contact details below). This information is being provided jointly by the following MAHs:

Table 1

Marketing Authorisation Holder	**Product Licence number**	**Product Name**	**Email**	**Telephone**
Accord Healthcare Ireland Ltd.	PA 2315/100/001 PA 2315/100/002 PA 2315/100/003	Ciplox (ciprofloxacin) 250 mg Film-coated Tablets Ciplox (ciprofloxacin) 500 mg Film-coated Tablets Ciplox (ciprofloxacin) 750 mg Film-coated Tablets	medinfo@accord-healthcare.com	+ 44 (0) 1271 385257
A. Menarini Industrie Farmaceutiche Riunite s.r.l.	EU/1/19/1393/002-007 EU/1/19/1393/001	Quofenix (delafloxacin) 450 mg Tablets Quofenix (delafloxacin) 300 mg Pdr/Conc/Soln for infusion	medinfo@menarini.ie	00 353 (1) 284 6744
Bluefish Pharmaceuticals AB	PA1436/019/001 PA1436/019/002	Levofloxacin Bluefish 250 mg Film-coated Tablets Levofloxacin Bluefish 500 mg Film-coated Tablets	drugreaction@bluefishpharma.com	+46 (0) 8 5191 1600
Chiesi Farmaceutici S.p.A	EU/1/14/973/001-002	Quinsair (levofloxacin) 240 mg Nebuliser solution	Pv.uk@chiesi.com	+44 (0) 161 488 5555
Clonmel Healthcare Ltd.	PA0126/203/001 PA0126/203/002	Profloxin (ciprofloxacin) 250 mg Film-coated Tablets Profloxin (ciprofloxacin) 500 mg Film-coated Tablets	medicalinformation@clonmel-health.ie	+353 52 617 7777
Fresenius Kabi Deutschland GmbH	PA 2059/010/001-002 PA 2059/013/001-002	Levofloxacin 5 mg/ml solution for infusion Moxifloxacin 400 mg/250 ml solution for infusion	Pharmacovigilance.gb@fresenius-kabi.com	+44 (0) 1928 533 575
Krka d.d. Novo mesto	PA1347/035/001 PA1347/035/002 PA1347/035/003 PA1347/048/001 PA1347/048/002	Ciprofloxacin Krka 250 mg Film-coated Tablets Ciprofloxacin Krka 500 mg Film-coated Tablets Ciprofloxacin Krka 750 mg Film-coated Tablets Levofloxacin Krka 250 mg Film-coated Tablets Levofloxacin Krka 500 mg Film-coated Tablets	pharmacovigilance.ie@krka.biz	+353 1 413 3710
McDermott Laboratories Ltd.	PA0577/069/001 PA0577/069/002	Cifloxager (ciprofloxacin) 250 mg Film-coated Tablets Cifloxager (ciprofloxacin) 500 mg Film-coated Tablets	pv.ireland@viatris.com	+44 (0) 800 121 8267

Marketing Authorisation Holder	Product Licence number	Product Name	Email	Telephone
	PA0577/104/002	Tavager (levofloxacin) 500 mg Film-coated Tablets		
Noridem Enterprises Ltd.	PA 1122/005-001 PA 1122/013/001	Ciprofloxacin 2 mg/ml Solution for infusion Levofloxacin 5 mg/ml Solution for infusion	pv@DEMO.GR	+30 210 816 1802
Pfizer Healthcare Ireland	PA 0822/237/001 PA 0822/237/002	Ciprofloxacin 2 mg/ml Solution for infusion	RegAffairsInfo@pfizer.com	+353 87 4322316
Rowex Ltd.	PA 0711/122/001 PA 0711/122/002 PA 0711/122/003	Cifox (ciprofloxacin) 250 mg Film-coated Tablets Cifox (ciprofloxacin) 500 mg Film-coated Tablets Cifox (ciprofloxacin) 750 mg Film-coated Tablets	pv@rowa-pharma.ie	+353 2750077
Sanofi-Aventis Ireland Ltd. T/A SANOFI	PA: 540/077/001 PA: 540/077/003	Tavanic (levofloxacin) 5 mg/ml Solution for infusion Tavanic (levofloxacin) 500 mg Film-coated Tablets	IEmedinfo@sanofi.com	+353 1 403 5600
Teva Pharma B.V.	PA 749/31/2 PA 749/31/3	Ciprofloxacin Teva 250 mg Film-coated Tablets Ciprofloxacin Teva 500 mg Film-coated Tablets	UK.Safety@tevauk.com	+44 (0) 207 540 7117

Yours faithfully,

Tony Rigden

Head of Regulatory and Pharmacovigilance

Chiesi Ltd.

Signed on behalf of the Marketing Authorisation Holders listed in table 1 above.