HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

# Fluoroquinolone antibiotics: Reminder about restrictions of use and risk of rare but serious long-lasting adverse reactions

Fluoroquinolones are a class of broad-spectrum antibiotics, which include the active substances ciprofloxacin, levofloxacin, and moxifloxacin*.

The European Medicines Agency (EMA) made strong recommendations to restrict the use of systemic and inhaled fluoroquinolones following an EU-wide review conducted in 2018[1]. The review evaluated the risk of serious and long-lasting (lasting months or years), disabling and potentially irreversible adverse reactions mainly affecting the musculoskeletal and nervous system, following which the EMA recommended significant restrictions on the use of fluoroquinolone medicines in 2019.

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.

The results from a recent EMA-funded study[2] ("Impact of European Union Label Changes for Fluoroquinolone Containing Medicinal Products for Systemic and Inhalation Use") suggest that despite the new restrictions introduced in 2019, fluoroquinolones are still potentially being used outside the authorised indications. The study involved an analysis of prescribing rates for fluoroquinolones in six European healthcare databases (Belgium, France, Germany, the Netherlands, Spain, and the United Kingdom). Due to the limitations of the study, no definitive conclusions can be drawn.

However, the EMA are reminding healthcare professionals (HCPs) of the existing advice to limit the use of these medicines to their approved indications after a careful assessment of the benefits and risks for individual patients. A Direct Healthcare Professional Communication[3] was issued in June 2023 outlining the restrictions on systemic and inhaled fluoroquinolone antibiotic use.

The HPRA previously published a special edition Drug Safety Newsletter (Edition 91)[4] highlighting all the primary outcomes from the 2018 EU-wide review, including recommendations for HCPs concerning fluoroquinolones and restrictions around their use.

*Advice to Healthcare Professionals*

- 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.

- 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.

**Key Message**

- Findings of a study commissioned by EMA (EUPAS37856)[2] suggest that fluoroquinolones are still potentially being used outside of their authorised indications.

- There are significant restrictions on the use of these medicines due to the risk of rare but long-lasting (up to months or years), serious, disabling and potentially irreversible adverse reactions affecting different, sometimes multiple, body systems (musculoskeletal, nervous, psychiatric and senses).

- Healthcare professionals are reminded that the use of systemic and inhaled fluoroquinolone is restricted following an EU-wide review[1], previously communicated in HPRA Drug Safety Newsletter (Edition 91)[4].

| *** Fluoroquinolone antibiotics authorised in Ireland are:** | |
|---|---|
| **Active Ingredient** | **Brand** |
| Ciprofloxacin | Ciprofloxacin Krka,Ciprofloxacin Noridem,Ciprofloxacin Pfizer, Ciprofloxacin Teva, Cifloxager, Cifox, Ciplox, Profloxin, Truoxin IV. |
| Levofloxacin | Levofloxacin Baxter, Levofloxacin Bluefish, Levofloxacin Fresenius Kabi Deutschland, Levofloxacin HikmaFarmaceutica, Levofloxacin Krka, Levofloxacin Noridem, Quinsair, Tavager, Tavanic. |
| Delafloxacin | Quofenix. |
| Moxifloxacin | Avelox, Moxifloxacin Fresenius Kabi Deutschland. |
| Further details available on www.hpra.ie and www.ema.europa.eu | |

**References:**


1. EU Review of Fluoroquinolones available at: https://www.ema.europa.eu/en/medicines/human/referrals/quinolone-fluoroquinolone-containing-medicinal-products
2. Impact of European Union Label Changes for Fluoroquinolone Containing Medicinal Products for Systemic and Inhalation Use (EUPAS37856) available at: https://www.encepp.eu/
3. Direct Healthcare Professional Communication, dated 8th June 2023, on important safety information for systemic and inhaled fluoroquinolone antibiotics available at: www.hpra.ie
4. HPRA Drug Safety Newsletter Edition 91 available at: www.hpra.ie