Direct Healthcare Professional Communication

Systemic and inhaled fluoroquinolone antibiotics – reminder on restrictions of use

<Active substance(s)>

Dear Healthcare Professional,

Marketing authorisation holders of fluoroquinolone antibiotics in agreement with the European Medicines Agency (EMA) and the <National Competent 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 European Medicines Agency (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

To be adapted according to national situation:

Call for reporting

Healthcare professionals are encouraged to report adverse events in patients taking fluoroquinolone antibiotics to [NCA] <*in accordance with the national spontaneous reporting system, including the details (e.g. name, postal address, fax number, website address) on how to access the national spontaneous reporting system*>

Company contact point

<A table of Marketing authorisation holders and contact point

Communication plan for Direct Healthcare professionals communication

DHPC COMMUNICATION PLAN	
Medicinal product(s)/active substance(s)	Ciprofloxacin Delafloxacin Levofloxacin Lomefloxacin Moxifloxacin Nadifloxacin Norfloxacin Ofloxacin Pefloxacin Prulifloxacin Rufloxacin For systemic and inhalation route
Marketing authorisation holder(s)	For full list of marketing authorisations holders, please refer to Annex I
Safety concern and purpose of the communication	**Systemic and inhaled fluoroquinolone antibiotics – risk of persistent serious side effects, reminder on restrictions of use**
DHPC recipients	Prescribing specialists (general practitioners, otorhinolaryngologists, specialists in internal medicine, pulmonologists, urologists, gynaecologists, intensive care physicians, surgeons, dermatologists, ophthalmologists, neurologists, orthopaedists, dentists especially periodontists, infectious disease specialists), community pharmacists, hospital pharmacists, professional societies, national associations. The NCAs should decide which specialties are relevant to receive the DHPC based on the national clinical practice. NCAs should also decide whether any other specialty should be added to the above list.
Member States where the DHPC will be distributed	Member States where the product is marketed.

Timetable	
DRAFT DHPC and communication plan (in English) agreed by PRAC	**14 April**
Consultation with MAHs	**28 April**
FINAL DHPC and communication plan (in English) agreed by PRAC	**12 May 2023**
Submission of translated DHPCs to the national competent authorities for review	**24 May 2023**
Agreement of translations by national competent authorities	**01 June 2023**
Dissemination of DHPC	**08 June 2023**