



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

16 November 2018
EMA/795349/2018

Disabling and potentially permanent side effects lead to suspension or restrictions of quinolone and fluoroquinolone antibiotics

EMA has reviewed serious, disabling and potentially permanent side effects with quinolone and fluoroquinolone antibiotics given by mouth, injection or inhalation. The review incorporated the views of patients, healthcare professionals and academics presented at EMA's public hearing on fluoroquinolone and quinolone antibiotics in June 2018.

EMA's human medicines committee (CHMP) has endorsed the recommendations of EMA's safety committee (PRAC) and concluded that the marketing authorisation of medicines containing cinoxacin, flumequine, nalidixic acid, and piperimidic acid should be suspended.

The CHMP confirmed that the use of the remaining fluoroquinolone antibiotics should be restricted. In addition, the prescribing information for healthcare professionals and information for patients will describe the disabling and potentially permanent side effects and advise patients to stop treatment with a fluoroquinolone antibiotic at the first sign of a side effect involving muscles, tendons or joints and the nervous system.

Restrictions on the use of fluoroquinolone antibiotics will mean that they should **not** be used:

- to treat infections that might get better without treatment or are not severe (such as throat infections);
- to treat non-bacterial infections, e.g. non-bacterial (chronic) prostatitis;
- for preventing traveller's diarrhoea or recurring lower urinary tract infections (urine infections that do not extend beyond the bladder);
- to treat mild or moderate bacterial infections unless other antibacterial medicines commonly recommended for these infections cannot be used.

Importantly, fluoroquinolones should generally be **avoided** in patients who have previously had serious side effects with a fluoroquinolone or quinolone antibiotic. They should be used **with special caution** in the elderly, patients with kidney disease and those who have had an organ transplantation because these patients are at a higher risk of tendon injury. Since the use of a corticosteroid with a fluoroquinolone also increases this risk, combined use of these medicines should be avoided.



The CHMP opinion will now be forwarded to the European Commission, which will issue a final legally binding decision applicable in all EU countries. National authorities will enforce this decision for the fluoroquinolone and quinolone medicines authorised in their countries and they will also take other appropriate measures to promote the correct use of these antibiotics.

Information for patients

- Fluoroquinolone medicines (which contain ciprofloxacin, levofloxacin, lomefloxacin, moxifloxacin, norfloxacin, ofloxacin, pefloxacin, prulifloxacin and rufloxacin) can cause long-lasting, disabling and potentially permanent side effects involving tendons, muscles, joints and the nervous system.
- These serious side effects include inflamed or torn tendon, muscle pain or weakness, and joint pain or swelling, walking difficulty, feeling pins and needles, burning pain, tiredness, depression, problems with memory, sleeping, vision and hearing, and altered taste and smell.
- Tendon swelling and injury may occur within 2 days of starting treatment with a fluoroquinolone but may even occur several months after stopping treatment.
- Stop taking a fluoroquinolone medicine and contact your doctor at once in the following cases:
 - at the first sign of tendon injury, such as tendon pain or swelling – rest the painful area;
 - if you get pain, feel pins and needles, tingling, tickling, numbness or burning, or weakness especially in the legs or arms;
 - if you get swelling in the shoulder, arms or legs, have walking difficulty, feel tired or depressed or have problems with your memory or with sleeping or you notice changes with your vision, taste, smell or hearing. You and your doctor will decide if you can continue treatment or if you need to take another type of antibiotic.
- You may be more prone to joint pain or swelling or tendon damage if you are aged over 60 years, your kidneys do not work well or you have received organ transplantation.
- Speak with your doctor if you are taking a corticosteroid (medicines such as hydrocortisone and prednisolone) or need to have treatment with a corticosteroid. You may be especially prone to tendon damage if you are taking a corticosteroid and a fluoroquinolone medicine at the same time.
- You should not take a fluoroquinolone medicine if you have ever had a serious side effect with a fluoroquinolone or a quinolone medicine and you should speak with your doctor immediately.
- If you have any questions or concerns about your medicines, speak to your doctor or pharmacist.

Information for healthcare professionals

- Fluoroquinolones are associated with prolonged (up to months or years), serious, disabling and potentially irreversible drug reactions affecting several, sometimes multiple, systems, organ classes and senses.
- The serious side effects include tendonitis, tendon rupture, arthralgia, pain in extremities, gait disturbance, neuropathies associated with paraesthesia, depression, fatigue, memory impairment, sleep disorders, and impaired hearing, vision, taste and smell.
- Tendon damage (especially to Achilles tendon but also other tendons) can occur within 48 hours of starting fluoroquinolone treatment but the damage may be delayed several months after stopping treatment.

- Patients who are older, have renal impairment or have had solid organ transplantation and those being treated with a corticosteroid are at higher risk of tendon damage. Concomitant treatment with a fluoroquinolone and a corticosteroid should be avoided.
- Fluoroquinolone treatment should be discontinued at the first sign of tendon pain or inflammation and patients should be advised to stop treatment with a fluoroquinolone and speak with the doctor in case of symptoms of neuropathy such as pain, burning, tingling, numbness or weakness so as to prevent development of potentially irreversible condition.
- Fluoroquinolones should generally not be used in patients who have had serious adverse reactions associated with the use of quinolone or fluoroquinolone medicines.
- Up-to-date summary of product characteristics should be consulted for authorised indications when considering treatment with a fluoroquinolone medicine. This is because the indications for these medicines have been restricted.
- The benefits and risks of fluoroquinolones will be monitored continuously and a drug utilisation study will evaluate the effectiveness of the new measures to reduce inappropriate use of fluoroquinolones by investigating changes in prescribing behaviour.

More about the medicine

Fluoroquinolones and quinolones are a class of broad-spectrum antibiotics that are active against bacteria of both Gram-negative and Gram-positive classes. Fluoroquinolones are of value in certain infections, including some life-threatening ones, where alternative antibiotics are not sufficiently effective.

The review covered medicines containing the following fluoroquinolone and quinolone antibiotics: cinoxacin, ciprofloxacin, flumequine, levofloxacin, lomefloxacin, moxifloxacin, nalidixic acid, norfloxacin, ofloxacin, pefloxacin, piperidic acid, prulifloxacin and rufloxacin.

The review concerned only medicines given systemically (by mouth or injection) and inhaled medicines.

More about the procedure

The review of fluoroquinolones and quinolones was initiated on 9 February 2017 at the request of the German medicines authority (BfArM), under [Article 31 of Directive 2001/83/EC](#).

The review was first carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines.

The final PRAC recommendations were adopted on 4 October 2018 and then sent to the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which adopted the Agency's opinion. The CHMP opinion will now be forwarded to the European Commission, which will issue a final legally binding decision applicable in all EU Member States.