
Fluoroquinolone antibiotics: reminder of measures to reduce the risk of long-lasting, disabling and potentially irreversible side effects

13/06/2023 | Circular Number P05/2023

Information on Fluoroquinolones

- Fluoroquinolone medicines are a family of broad-spectrum antibiotics that kill bacteria and fight infections. They are used to treat certain types of serious infections when other antibiotics are not suitable.
- The EU-wide review, conducted in 2018 by EMA, concerned fluoroquinolone medicines given systemically (by mouth or injection) and inhaled medicines and covered medicines containing ciprofloxacin, flumequine, levofloxacin, lomefloxacin, moxifloxacin, norfloxacin, ofloxacin, pefloxacin, prulifloxacin and rufloxacin. Fluoroquinolone medicines are authorised in various EU Member States under different trade names.

In Malta four different fluoroquinolone antibiotics are authorised through national and centralised procedures. These are ciprofloxacin, levofloxacin, moxifloxacin, delafloxacin and norfloxacin. For more details on fluoroquinolone containing products authorised in Malta refer to [Annex I](#) at the end of this document.

Information from the EMA about the safety concern

- EMA's safety committee, PRAC, is reminding healthcare professionals that the use of fluoroquinolone antibiotics, given by mouth, injection or inhalation, is restricted due to the risk of disabling, long-lasting and potentially irreversible side effects.
- These restrictions were introduced in 2019 following an [EU-wide review](#) of these very rare, but serious side effects. An EMA funded study¹ has shown that although the use of fluoroquinolone antibiotics has reduced, these medicines may still be prescribed outside of their recommended uses.
- Restrictions on the use of fluoroquinolone antibiotics 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);

¹ "Impact of European Union Label Changes for Fluoroquinolone Containing Medicinal Products for Systemic and Inhalation Use" ([EUPAS37856](#))

- to treat mild or moderate bacterial infections unless other antibacterial medicines commonly recommended for these infections cannot be used.
- Importantly, fluoroquinolones should 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 in 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 study², which evaluated data from the primary care setting in six European countries (Belgium, France, Germany, the Netherlands, Spain and the United Kingdom) between 2016 and 2021, suggests that the measures taken to restrict the use of these medicines as a result of the EU-wide review had a modest impact.
- A Direct Healthcare Professional Communication (DHPC) will now be sent to healthcare professionals in the EU. The DHPC will emphasise the need to limit the use of these medicines to a last-line treatment in patients who have no alternative therapeutic options and only after a careful assessment of the benefits and risks for individual patients.

Information for patients

Fluoroquinolone antibiotics can cause serious side effects involving the nervous system, tendons, muscles and joints. Your doctor should only prescribe these medicines when there are no other suitable options.

- These very rare, but serious side effects include inflamed or torn tendons, muscle pain or weakness, joint pain or swelling, difficulty walking, 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.
- If you are over 60 years of age, have a history of kidney problems or have had an organ transplantation, or if you are taking a corticosteroid (medicines such as prednisolone or hydrocortisone), you have a greater risk of developing tendon damage with a fluoroquinolone.
- If you experience the following side effects, stop treatment, and contact your doctor immediately:
 - tendon pain or swelling, particularly in the ankle or calf. If this happens, rest the painful area;
 - pain, numbness, tingling, swelling, or muscle weakness in different parts of the body, often beginning in the hands or feet, that gets worse over time;
 - severe tiredness, depression, poor memory or severe problems sleeping;

² "Impact of European Union Label Changes for Fluoroquinolone Containing Medicinal Products for Systemic and Inhalation Use" ([EUPAS37856](#))

- changes in vision, hearing, taste and smell;
- swelling in your shoulders, arms or legs, or pains in your joints.

You and your doctor will decide if you can continue treatment or if you need another type of antibiotic

- You should not take a fluoroquinolone medicine if you have ever had a serious side effect with a fluoroquinolone or a quinolone medicine.
- If you have any questions or concerns about your medicines, speak to your doctor or pharmacist.

In Malta

Information for healthcare professionals

- Findings of a study commissioned by EMA ([EUPAS37856](#)) suggest that fluoroquinolones continue to be prescribed outside of their recommended uses.
- EMA also notes that the study was subject to limitations and that caution should therefore be used when interpreting its data.
- Healthcare professionals are reminded of the outcome of an [EU-wide review](#) of inhaled and systemic quinolone and fluoroquinolone antibiotics that was conducted in 2018 by EMA. This review led to 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).
- These adverse reactions can be limited by restricting the use of fluoroquinolones to a last-line treatment in patients who have no alternative therapeutic options and only after a careful assessment of the benefits and risks for individual patients.
- Particular caution should be taken when prescribing fluoroquinolones in older patients, those with renal impairment, solid organ transplantation or on systemic corticosteroids as the risk of some adverse reactions (e.g. tendonitis, tendon rupture) are higher in these patients. Concomitant treatment with a fluoroquinolone and a corticosteroid should be avoided.
- Patients should be informed of the risks associated with fluoroquinolones prior to initiating treatment, including the potentially long-lasting and serious nature of these side effects, and advised to stop treatment and speak with their doctor at the first signs or symptoms of these adverse reactions.
- Fluoroquinolone treatment should be discontinued, and alternative treatment should be considered at the first sign of tendon pain or inflammation or of symptoms of neuropathy such as pain, burning, tingling, numbness, or weakness, so as to prevent development of potentially irreversible adverse reactions.

Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance with fluoroquinolones. Suspected Adverse Drug Reactions (side effects) may be reported using the Medicines Authority Form and sending it to: Sir Temi Zammit Buildings, Malta Life Sciences Park, San Gwann SGN 3000 or online to <http://www.medicinesauthority.gov.mt/adrportal> or to the marketing authorisation holder or their local representatives.

Post-Licensing Directorate

Medicines Authority

Healthcare professionals and patients are encouraged to regularly check the Medicines Authority website for product safety updates as these are issued on an ongoing basis.

Annex 1

Active ingredients	Medicine Name	Pharmaceutical Forms	Classification	Authorisation Number	Authorization Holder	Status
Ciprofloxacin 250 milligram(s)	Zindolin 250 Tablets	Film-coated tablet	POM	MA084/02601	Remedica Limited	A*
Ciprofloxacin Hydrochloride 250 milligram(s)	Viprolox 250mg Film coated tablets	Film-coated tablet	POM	MA115/00501	Delorbis Pharmaceuticals Limited	A*
Ciprofloxacin 250 milligram(s)	Sepcen Film-coated Tablets 250mg	Film-coated tablet	POM	MA120/00202	Especialidades Farmaceuticas Centrium SA	A*
Ciprofloxacin 250 milligram(s)	Medociprin	Film-coated tablet	POM	MA032/01802	Medochemie Limited	A*
Ciprofloxacin 250 milligram(s)	Ciprinol 250 mg film-coated tablets	Film-coated tablet	POM	PI908/22703A	NeoFarma Pharmaceuticals Limited	A*
Ciprofloxacin Hydrochloride 250 milligram(s)	Profloxin Tablet, film coated 250mg	Film-Coated Tablet	POM	AA1045/03303	Clonmel Healthcare Limited	A*
Ciprofloxacin 250 milligram(s)	Ciprofloxacin Aurobindo Tablet, film coated 250mg	Film-Coated Tablet	POM	AA565/06005	Central Procurement & Supplies Unit	A*
Ciprofloxacin 250 milligram(s)	Ciprofloxacin Teva 250 mg Film-coated Tablets	Film-coated tablet	POM	AA1438/00802	NM Pharma Limited	A*
Ciprofloxacin 250 milligram(s)	Ciprinol 250 mg film-coated tablets	Film-coated tablet	POM	MA982/02601	TAD Pharma GmbH	A*
Ciprofloxacin 250 milligram(s)	Ciprofloxacin Teva 250mg film-coated Tablets	Film-coated tablet	POM	AA908/17501	NeoFarma Pharmaceuticals Limited	A*
Ciprofloxacin 250 milligram(s)	Ciplox 250 mg film-coated tablets	Film-coated tablet	POM	AA770/16001	JV Healthcare Limited	A*
Ciprofloxacin 250 milligram(s)	Ciprofloxacin Mylan 250mg film-coated tablets	Film-coated tablet	POM	AA1438/00803	NM Pharma Limited	A*
Norfloxacin 400 milligram(s)	Norfloxacin EG 400 mg Film-coated tablets	Film-coated tablet	POM	AA565/93901	Central Procurement & Supplies Unit	A*
Norfloxacin 400 milligram(s)	Norfloxacin ABC 400 mg hard capsules	Hard capsules	POM	AA565/93902	Central Procurement & Supplies Unit	A*
Moxifloxacin 400 milligram(s)	Moxifloxacin 400mg film-coated Tablets	Film-coated tablet	POM	AA565/43801	Central Procurement & Supplies Unit	A*

Active ingredients	Medicine Name	Pharmaceutical Forms	Classification	Authorisation Number	Authorization Holder	Status
Moxifloxacin 400 milligram(s)	Moxifloxacin 400mg film-coated Tablets	Film-coated tablet	POM	AA565/43802	Central Procurement & Supplies Unit	A*
Norfloxacin 400 milligram(s)	Trizolin 400 Tablet, film coated 400mg	Film-coated tablet	POM	AA084/09801	Remedica Limited	A*
Norfloxacin 400 milligram(s)	Norfloxacin Helcor 400 mg film-coated tablets	Film-coated tablet	POM	AA729/30401	Cherubino Limited	A*
Norfloxacin 400 milligram(s)	Uroflox, 400 mg, film-coated tablets	Film-coated tablet	POM	AA565/91301	Central Procurement & Supplies Unit	A*
Moxifloxacin 400 milligram(s)	Erelan Tablet, film coated 400mg	Film-coated tablet	POM	MA032/12001	Medochemie Limited	A*
Ciprofloxacin 500 milligram(s)	Medociprin	Film-coated tablet	POM	MA032/01801	Medochemie Limited	A*
Ciprofloxacin 500 milligram(s)	Ciproxin 500mg Film-coated Tablets	Tablet	POM	MA639/01702	Bayer PLC	A*
Ciprofloxacin 500 milligram(s)	Viprolox 500mg Film-coated tablets	Film-coated tablet	POM	MA115/00502	Delorbis Pharmaceuticals Limited	A*
Ciprofloxacin 500 milligram(s)	Sepcen Film-coated Tablets 500mg	Film-coated tablet	POM	MA120/00201	Especialidades Farmaceuticas Centrium SA	A*
Ciprofloxacin 500 milligram(s)	Ciproxin 500mg Film-Coated Tablets	Film-coated tablet	POM	PI908/02903A	NeoFarma Pharmaceuticals Limited	A*
Ciprofloxacin Hydrochloride 500 Milligram(S)	Cifox Tablet, film coated 500mg	Film-coated tablet	POM	AA1122/00202	Rowex Ltd	A*
Ciprofloxacin Hydrochloride 500 milligram(s)	Profloxin Tablet, film coated 500mg	Film-Coated Tablet	POM	AA1045/03304	Clonmel Healthcare Limited	A*
Levofloxacin 500 milligram(s)	Tavanic 500mg film-coated tablet	Film-coated tablet	POM	MA1359/03801	Sanofi Malta Limited	A*
Levofloxacin 500 milligram(s)	AMESOL 500mg Film-Coated Tablets	Film-coated tablet	POM	AA032/09101	Medochemie Limited	A*
Levofloxacin 500 milligram(s)	Tavanic Coated Tablets 500mg	Film-coated tablet	POM	PI908/07801A	NeoFarma Pharmaceuticals Limited	A*
Ciprofloxacin 500 milligram(s)	Ciprofloxacin Teva 500mg film-coated Tablets	Film-coated tablet	POM	AA908/17502	NeoFarma Pharmaceuticals Limited	A*

Active ingredients	Medicine Name	Pharmaceutical Forms	Classification	Authorisation Number	Authorization Holder	Status
Levofloxacin 500 milligram(s)	Levofloxacin 500mg Film-coated Tablets	Film-coated tablet	POM	AA565/24102	Central Procurement & Supplies Unit	A*
Levofloxacin 500 milligram(s)	Levofloxacin Tablet, film coated 500mg	Film-coated tablet	POM	AA565/24102	Central Procurement & Supplies Unit	A*
Ciprofloxacin 500 milligram(s)	Ciprofloxacin Teva 500 mg Film-coated Tablets	Film-coated tablet	POM	AA1438/00801	NM Pharma Limited	A*
Ciprofloxacin 500 milligram(s)	Ciprinol 500 mg film-coated tablets	Film-coated tablet	POM	MA982/02602	TAD Pharma GmbH	A*
Ciprofloxacin 500 milligram(s)	Ciprinol 500 mg film-coated tablets	Film-coated tablet	POM	PI908/22704A	NeoFarma Pharmaceuticals Limited	A*
Ciprofloxacin 500 milligram(s)	Ciplox 500 mg film-coated tablets	Film-coated tablet	POM	AA770/16002	JV Healthcare Limited	A*
Levofloxacin 500 milligram(s)	Floxaval 500mg Film-coated tablets	Film-coated tablet	POM	AA115/02101	Delorbis Pharmaceuticals Limited	A*
Ciprofloxacin 500 milligram(s)	Ciprofloxacin Mylan 500mg film-coated tablets	Film-coated tablet	POM	AA1438/00804	NM Pharma Limited	A*
Levofloxacin 500 milligram(s)	Levofloxacin Arena 500 mg film-coated tablets	Film-coated tablet	POM	AA1161/02201	Farmarosib SRL	A*
Ciproxin 250 milligram(s)	Ciproxin 250 mg/5 mL granules and solvent for oral suspension	Granules and solvent for oral suspension	POM	AA565/09903UK	Central Procurement & Supplies Unit	A*
Ciprofloxacin 2 milligram(s)/millilitre	Ciprofloxacin Kabi 400 mg/200 ml solution for infusion	Solution for infusion	POM	MA1123/03802	Fresenius Kabi Italia S.r.l.	A*
Levofloxacin 5 milligram(s)/millilitre	Levofloxacin Ibigen 5 mg/ml solution for infusion (50ml vial)	Solution for infusion	POM	MA965/00101	Ibigen S.r.l.	A*
Levofloxacin 500 milligram(s)	Levofloxacin Ibigen 5 mg/ml solution for infusion (100ml vial)	Solution for infusion	POM	MA965/00102	Ibigen S.r.l.	A*
Levofloxacin 5 milligram(s)/millilitre	Levofloxacin Solution for Infusion 5mg/ml	Solution for infusion	POM	AA1124/00201	Noridem Enterprises Ltd	A*

Active ingredients	Medicine Name	Pharmaceutical Forms	Classification	Authorisation Number	Authorization Holder	Status
Moxifloxacin	Moxifloxacin Anfarm 400 mg/250 ml	Solution for infusion	POM	MA240/02201	Anfarm Hellas S.A.	A*
Moxifloxacin	Avelox 400mg/250ml solution for infusion	Solution for infusion	POM	MA639/01602	Bayer PLC	A*
Ciprofloxacin 2 milligram(s)/millilitre	Reviorm Solution for Infusion 200mg/100ml	Solution for infusion	POM	AA1025/01001	Norma Hellas S.A.	A*
Ciprofloxacin 2 milligram(s)/millilitre	Nafloxin Injectable Solution for Infusion 200mg/100ml	Solution for infusion	POM	AA1001/00801	COOPER S.A. Pharmaceuticals	A*
Ciprofloxacin 2 milligram(s)/millilitre	Ciprofloxacin Solution for Infusion 2mg/ml	Solution for infusion	POM	AA1124/00102	Noridem Enterprises Ltd	A*
Ciprofloxacin 2 milligram(s)/millilitre	Ciprofloxacin Kabi 200mg/100ml solution for infusion	Solution for infusion	POM	AA1123/03801	Fresenius Kabi Italia S.r.l	A*
Levofloxacin 5 milligram(s)/millilitre	Levofloxacin Solution for Infusion 5mg/ml	Solution for infusion	POM	MA1123/01501	Fresenius Kabi Italia S.r.l	A*
Levofloxacin 5 milligram(s)/millilitre	Levofloxacin Ibigen Solution for Infusion 5mg/ml (50ml vial)	Solution for infusion	POM	MA965/00101	Ibigen S.r.L	A*
Delafloxacin 25 milligram(s)/millilitre	Delafloxain powder for concentrate for solution for infusion 25 mg/ml (50ml vial)	Powder for concentrate for solution for infusion	POM	EMA/H/C/00486 0	A. Menarini Industrie Farmaceutiche Riunite s.r.l.	A*

*A - Authorised

Feedback Form

The Medicines Authority thanks you for the time taken to read this safety circular. The dissemination of safety circulars is an important process whereby Regulatory Authorities can communicate important issues with respect to the safety of medicines, in order to protect and enhance public health.

The Medicines Authority kindly invites your anonymous feedback about the regulatory action being communicated. This may be returned by folding this form (address side up), stapling the ends and then posting (no stamp required).

Feedback:

We thank you for your interest and look forward to hearing your opinion.

Postage will be paid
by the Licensee

No postage stamp
necessary if posted
in Malta and Gozo

BUSINESS REPLY SERVICE

Licence no. 656

Pharmacovigilance Section
Post-Licensing Directorate
Medicines Authority
Sir Temi Żammit Buildings
Malta Life Sciences Park
San Ġwann SĠN 3000