
Quinolone and Fluoroquinolone antibiotics: use restricted due to disabling and potentially permanent side effects

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Information on quinolone and fluoroquinolone antibiotics

- Quinolones and fluoroquinolones are a class of broad-spectrum antibiotics, 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 the following medicines: ciprofloxacin, flumequine, levofloxacin, lomefloxacin, moxifloxacin, norfloxacin, ofloxacin, pefloxacin, prulifloxacin and rufloxacin (fluoroquinolone antibiotics); cinoxacin, nalidixic acid, pipemidic acid (quinolone antibiotics)
- The review concerned only medicines given systemically (by mouth or injection) and inhaled medicines

In Malta four different fluoroquinolone antibiotics are authorised through national procedures. These are ciprofloxacin, levofloxacin, moxifloxacin 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 quinolones and fluoroquinolones use restriction

The EMA decided to suspend the marketing authorisations of medicines containing cinoxacin, flumequine, nalidixic acid, and pipemidic acid following PRAC's recommendations and recommended to restrict the use of the remaining fluoroquinolone antibiotics. In addition, the prescribing information for healthcare professionals and the information for patients will be amended to include 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.

Following EMA's recommendations, fluoroquinolones 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
- To treat patients who already experienced side effects with a fluoroquinolone or quinolone antibiotic
- In combination with corticosteroids due to an increased risk of side effects

Quinolone and fluoroquinolone antibiotics 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
- In patient who experienced serious side effects with quinolones and fluoroquinolones

The European Commission issued a final legally binding decision on quinolone and fluoroquinolone antibiotics given by mouth and by injection, which is applicable in all EU Member States.

In Malta

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

A DHPC letter about the safety concern has been disseminated to HCPs in Malta. Archived DHPC letters are available online at <http://www.medicinesauthority.gov.mt/dhpc>

Advice for Patients

- Fluoroquinolone medicines (which contain ciprofloxacin, levofloxacin, lomefloxacin, moxifloxacin, norfloxacin, ofloxacin, pefloxacin, prulifloxacin and rifloxacin) 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.

For more information, please visit the European Medicines Agency's [quinolone and fluoroquinolone containing medicinal products referral page](#)

Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance on quinolone and fluoroquinolone antibiotics. Suspected Adverse Drug Reactions (side effects) may be reported using the Medicines Authority Form and sending it to Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 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 I

Active ingredients	Medicine Name	Pharmaceutical Forms	Classification	Authorisation Number	Authorization Holder	Status
Ciprofloxacin 500 milligram(s)	Medociprin	Film-coated tablet	POM	MA032/01801	Medochemie Limited	A*
Ciprofloxacin 250 milligram(s)	Medociprin	Film-coated tablet	POM	MA032/01802	Medochemie Limited	A*
Ciprofloxacin 250 milligram(s)	Ciproxin 250mg Film-coated Tablets	Tablet	POM	MA513/00703	Bayer PLC	A*
Ciprofloxacin 500 milligram(s)	Ciproxin 500mg Film-coated Tablets	Tablet	POM	MA513/00704	Bayer PLC	A*
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 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 250 milligram(s)	Sepcen Film-coated Tablets 250mg	Film-coated tablet	POM	MA120/00202	Especialidades Farmaceuticas Centrium SA	A*
Ciprofloxacin 500 milligram(s)	Siprox 500mg film coated tablets	Film-coated tablet	POM	MA628/17902	Actavis Group PTC ehf	A*
Ciprofloxacin 250 milligram(s)	Siprox 250mg film coated tablets	Film-coated tablet	POM	MA628/17901	Actavis Group PTC ehf	A*
Ciprofloxacin 250 milligram(s)	Aristin-C	Film-coated tablet	POM	MA240/00101	Anfarm Hellas S.A.	A*
Ciprofloxacin 500 milligram(s)	Aristin-C	Film-coated tablet	POM	MA240/00102	Anfarm Hellas S.A.	A*
Ciprofloxacin 200 milligram(s)	Aristin-C	Solution for infusion	POM	MA240/00103	Anfarm Hellas S.A.	A*
Ciprofloxacin 200 milligram(s)	Ciproxin Solution for Infusion 200mg/100ml	Solution for infusion	POM	MA513/00705	Bayer PLC	A*
Ciprofloxacin 100 milligram(s)	Ciprofloxacin Ibigen 100mg/50ml solution for infusion	Solution for infusion	POM	MA965/00201	Ibigen S.r.L	A*
Ciprofloxacin 200 milligram(s)	Ciprofloxacin Ibigen 200mg/100ml solution for infusion	Solution for infusion	POM	MA965/00202	Ibigen S.r.L	A*
Ciprofloxacin 400 milligram(s)	Ciprofloxacin Ibigen 400mg/200ml solution for infusion	Solution for infusion	POM	MA965/00203	Ibigen S.r.L	A*
Ciprofloxacin 500 milligram(s)	Ciproxin 500mg Film-Coated Tablets	Film-coated tablet	POM	PI908/02901A	NeoFarma Pharmaceuticals Limited	A*
Ciprofloxacin 500 milligram(s)	Ciproxin Film-coated Tablets 500mg	Film-coated tablet	POM	PI555/04302A	Ecosse Limited	A*
Ciprofloxacin 250 milligram(s)	Ciproxin Tablets 250mg	Film-coated tablet	POM	PI908/02902A	NeoFarma Pharmaceuticals Limited	A*
Ciprofloxacin 250 milligram(s)	Ciprofloxacin 250mg Film-Coated Tablets	Film-coated tablet	POM	AA054/04901	Accord Healthcare Limited	A*

Active ingredients	Medicine Name	Pharmaceutical Forms	Classification	Authorisation Number	Authorization Holder	Status
Ciprofloxacin 2 milligram(s)/millilitre	Revionorm Solution for Infusion 200mg/100ml	Solution for infusion	POM	AA1025/01001	Norma Hellas S.A.	A*
Ciprofloxacin 2 milligram(s)/millilitre	Ciprofloxacin 2mg/ml solution for infusion	Solution for infusion	POM	AA292/00501	Villerton Invest S.A.	A*
Ciprofloxacin 250 milligram(s)	Ciprinol 250mg film-coated Tablets	Film-coated tablet	POM	AA604/01101	KRKA DD Novo Mesto	A*
Ciprofloxacin 500 milligram(s)	Ciprinol 500mg film-coated Tablets	Film-coated tablet	POM	AA604/01102	KRKA DD Novo Mesto	A*
Ciprofloxacin 250 milligram(s)	Ciprolen Tablet, film coated 250mg	Film-coated tablet	POM	AA984/00301	S.C. AC Helcor Pharma S.R.L.	A*
Ciprofloxacin 500 milligram(s)	Ciprolen Tablet, film coated 500mg	Film-coated tablet	POM	AA984/00302	S.C. AC Helcor Pharma S.R.L.	A*
Ciprofloxacin 250 milligram(s)	Ciproxin Tablets 250mg	Tablet	POM	PI555/04301A	Ecosse Limited	A*
Ciprofloxacin Lactate 2 milligram(s)/millilitre	Ciprofloxacin 2mg/ml, Solution for Infusion	Solution for infusion	POM	AA244/20902	P & D Pharmaceuticals Limited	A*
Ciprofloxacin 2 milligram(s)/millilitre	Ciprofloxacin Solution for Infusion 2mg/ml	Solution for infusion	POM	AA565/06003	Central Procurement & Supplies Unit	A*
Ciprofloxacin 250 milligram(s)	Ciprofloxacin 250mg Film-coated Tablets	Film-coated tablet	POM	AA565/06002	Central Procurement & Supplies Unit	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 250 milligram(s)/5 millilitre	Ciproxin Granules and Solvent for Oral Suspension 250mg/5ml	Granules for oral suspension	POM	AA565/09901	Central Procurement & Supplies Unit	A*
Ciprofloxacin lactate 2 milligram(s)/millilitre	Ciprofloxacin 2mg/ml Solution for Infusion	Solution for infusion	POM	AA1107/00201	Claris Lifesciences UK Limited	A*
Ciprofloxacin 2 milligram(s)/millilitre	Nafloxin Solution for Infusion 200mg/100ml	Solution for infusion	POM	AA729/15301	Cherubino Limited	A*
Ciprofloxacin hydrochloride 250 milligram(s)	Cifox Tablet, film coated 250mg	Film-coated tablet	POM	AA1122/00201	Rowex Ltd	A*
Ciprofloxacin Hydrochloride 500 Milligram(S)	Cifox Tablet, film coated 500mg	Film-coated tablet	POM	AA1122/00202	Rowex Ltd	A*
Ciprofloxacin Hydrochloride 750 milligram(s)	Cifox Tablet, film coated 750mg	Film-coated tablet	POM	AA1122/00203	Rowex Ltd	A*
Ciprofloxacin 2 milligram(s)/millilitre	Ciprofloxacin Solution for Infusion 2mg/ml	Solution for infusion	POM	AA1124/00101	Noridem Enterprises Ltd	A*
Ciprofloxacin Hydrochloride 250 milligram(s)	Profloxin Tablet, film coated 250mg	Film-Coated Tablet	POM	AA1045/03301	Clonmel Healthcare Limited	A*
Ciprofloxacin Hydrochloride 500 milligram(s)	Profloxin Tablet, film coated 500mg	Film-Coated Tablet	POM	AA1045/03302	Clonmel Healthcare Limited	A*
Ciprofloxacin 500 milligram(s)	Ciproxin Tablet, film coated 500mg	Film-Coated Tablet	POM	PI521/07701A	Medicem Limited	A*
Ciprofloxacin 250 milligram(s)	Ciprofloxacin Tablet, film coated 250mg	Film-Coated Tablet	POM	AA565/06004	Central Procurement & Supplies Unit	A*

Active ingredients	Medicine Name	Pharmaceutical Forms	Classification	Authorisation Number	Authorization Holder	Status
Ciprofloxacin 2 milligram(s)/millilitre	Ciprofloaxcin Solution for Infusion 2mg/ml	Solution for infusion	POM	AA729/07902	Cherubino Limited	A*
Ciprofloxacin 2 milligram(s)/millilitre	Ciprofloxacin Kabi 200mg/100ml solution for infusion	Solution for infusion	POM	AA1123/00601	Fresenius Kabi Italia S.r.l	A*
Ciprofloxacin 2 milligram(s)/millilitre	Ciprofloxacin Solution for Infusion 2mg/ml	Solution for infusion	POM	AA1124/00102	Noridem Enterprises Ltd	A*
Ciprofloxacin 250 milligram(s)	Ciprofloxacin Tablet, film coated 250mg	Film-Coated Tablet	POM	AA1173/02101	Medical Logistics Ltd	A*
Ciprofloxacin 500 milligram(s)	Ciprofloxacin Tablet, film coated 500mg	Film-Coated Tablet	POM	AA1173/02102	Medical Logistics Ltd	A*
Levofloxacin 500 milligram(s)	Tavanic 500mg film-coated tablet	Film-coated tablet	POM	MA082/03502	Sanofi Malta Limited	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 250 milligram(s)	Levoxa 250mg film-coated Tablets	Film-coated tablet	POM	MA628/00501	Actavis Group PTC ehf	A*
Levofloxacin 500 milligram(s)	Levoxa 500mg film-coated Tablets	Film-coated tablet	POM	MA628/00502	Actavis Group PTC ehf	A*
Levofloxacin 5 milligram(s)/millilitre	Levofloxacin Solution for Infusion 5mg/ml (50ml vial)	Solution for infusion	POM	MA628/04501	Actavis Group PTC ehf	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*
Levofloxacin 250 milligram(s)	Levofloxacin 250mg Film-coated Tablets	Film-coated tablet	POM	AA054/07301	Accord Healthcare Limited	A*
Levofloxacin 500 milligram(s)	Levofloxacin 500mg Film-coated Tablets	Film-coated tablet	POM	AA054/07302	Accord Healthcare 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*
Levofloxacin 500 milligram(s)	Floxaval 500mg Film-coated tablets	Film-coated tablet	POM	AA115/02101	Delorbis Pharmaceuticals Limited	A*
Levofloxacin 500/100 milligram(s)/millilitre	Levofloxacin/cooper 500mg/100ml solution for I.V.	Solution for infusion	POM	AA1001/00901	COOPER S.A. Pharmaceuticals	A*
Levofloxacin 5 milligram(s)	Levofloxacin Solution for Infusion 5mg/ml	Solution for infusion	POM	AA244/40501	P & D Pharmaceuticals Limited	A*
Levofloxacin 5 milligram(s)	Levofloxacin Solution for Infusion 5mg/ml	Solution for infusion	POM	PI244/40502A	P & D Pharmaceuticals Limited	A*
Levofloxacin 5 milligram(s)/millilitre	Levofloxacin Solution for Infusion 5mg/ml (100ml vial)	Solution for infusion	POM	MA628/04502	Actavis Group PTC ehf	A*
Levofloxacin 500 milligram(s)	Levofloxacin 500mg Film-coated Tablets	Film-coated tablet	POM	AA565/24101	Central Procurement & Supplies Unit	A*

Active ingredients	Medicine Name	Pharmaceutical Forms	Classification	Authorisation Number	Authorization Holder	Status
Levofloxacin 500 milligram(s)	Trissil 500mg film-coated tablets	Film-coated tablet	POM	AA037/00802	PIAM Farmaceutici S.p.A.	A*
Levofloxacin 500 milligram(s)	Levofloxacin Tablet, film coated 500mg	Film-coated tablet	POM	AA565/24102	Central Procurement & Supplies Unit	A*
Levofloxacin 500 milligram(s)	Levofloxacin Ibigen Solution for Infusion 5mg/ml (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*
Moxifloxacin 400 milligram(s)	Avelox 400mg film-coated Tablets	Film-coated tablet	POM	MA513/02701	Bayer PLC	A*
Moxifloxacin 400 milligram(s)	Avelox 400mg/250ml solution for infusion	Solution for infusion	POM	MA513/02702	Bayer PLC	A*
Moxifloxacin 400 milligram(s)	Erelan Tablet, film coated 400mg	Film-coated tablet	POM	MA032/12001	Medochemie Limited	A*
Norfloxacin 400 milligram(s)	Fluseminal	Film-coated tablet	POM	MA240/00401	Anfarm Hellas S.A.	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.

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