

Direct Healthcare Professional Communication

**Systemic and inhaled quinolones and fluoroquinolones antibiotics: restriction of use and recommendations to reduce risk of disabling, irreversible adverse events**

Dear Healthcare professional,

Actavis Group PTC ehf, Bayer plc, Beximco Pharmaceuticals Ltd, BIAL – Portela & C S.A. Chiesi Farmaceutici S.p.A., Claris Lifesciences UK Limited, Clonmel Healthcare Limited, COOPER S.A. Pharmaceuticals, Delorbis Pharmaceuticals Ltd, Europharma Ltd, Fresenius Kabi Italia S.r.l., Ibigen S.r.L, KRKA, d. d., Novo Mesto, Medical Logistics Ltd., Medicem Limited, Neofarma Pharmaceuticals Ltd, Noridem Enterprises Ltd., Norma Hellas S.A, P and D Pharmaceuticals Limited, PIAM Farmaceutici S.p.A., Remedica Limited, Rowex Ltd, Sanofi Malta Ltd, S.C. AC Helcor S.R.L., TAD Pharma GmbH, Villerton Invest S.A.in agreement with the European Medicines Agency and the Malta Medicines Authority, would like to inform you of the following:

**Summary**

- **Disabling, long-lasting and potentially irreversible adverse reactions mainly affecting musculoskeletal and nervous systems have been reported with quinolone and fluoroquinolone antibiotics**
- **As a consequence, the benefits and risks of all quinolone and fluoroquinolone antibiotics and their indications across the EU were reviewed**
- **The medicinal products containing cinoxacin, flumequine, nalidixic acid and piperidic acid will be removed from the market**
- **Do not prescribe these medicines**
  - **for treating non-severe or self-limiting infections (such as pharyngitis, tonsillitis and acute bronchitis)**
  - **for preventing travellers' diarrhoea or recurrent lower urinary tract infections**
  - **for non-bacterial infections, e.g. non-bacterial (chronic) prostatitis**
  - **for 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.**
  - **for patients who have previously had serious adverse reactions with a quinolone or fluoroquinolone antibiotic**
- **Prescribe these medicines with special caution for the elderly, patients with renal impairment, patients with solid organ transplants, and those concurrently treated with corticosteroids, as the risk of fluoroquinolone-induced tendinitis and tendon rupture may be exacerbated in these patients. Concomitant use of corticosteroids with fluoroquinolones should be avoided**
- **Advise patients to stop treatment at the first signs of a serious adverse reaction, such as tendinitis and tendon rupture, muscle pain, muscle weakness, joint pain, joint swelling, peripheral neuropathy and central nervous system effects and to contact their doctor for further advice.**

## Background to safety concern

EMA has reviewed systemic and inhaled quinolone and fluoroquinolone antibiotics to evaluate the risk of serious, long-lasting (lasting months or years), disabling and potentially irreversible adverse reactions that mainly affect the musculoskeletal and nervous systems.

Serious adverse reactions of the musculoskeletal system include tendinitis, tendon rupture, myalgia, muscle weakness, arthralgia, joint swelling and gait disturbance.

Serious peripheral and central nervous system effects include peripheral neuropathy, insomnia, depression, fatigue, memory impairment, as well as impairment of vision, hearing, smell and taste.

Only a few cases of these disabling and potentially irreversible adverse reactions have been reported, but underreporting can be assumed. Due to the seriousness of these reactions in previously healthy persons, any decision to prescribe quinolones and fluoroquinolones should be taken after a careful assessment of the benefits and risk in each case.

The product information for fluoroquinolone-containing medicines will be updated with this new information. The product information of fluoroquinolones is also being updated to include the risk of aortic aneurysm and dissection as communicated in joint DHPC, 06/2018/FS, published in October 2018.

## Further information

For further information, please visit the EMA website at: <https://www.ema.europa.eu/en/medicines/human/referrals/quinolone-fluoroquinolone-containing-medicinal-products>

Archived DHPC letters are available online at: <http://www.medicinesauthority.gov.mt/dhpc>

## Call for reporting

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are reminded to continue to report suspected adverse reactions associated with quinolone and fluoroquinolone antibiotics in accordance with the national spontaneous reporting system. Report forms can be downloaded from [www.medicinesauthority.gov.mt/adrportal](http://www.medicinesauthority.gov.mt/adrportal) and posted to Post-licensing directorate, Medicines Authority, Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000, Malta or sent by email to [postlicensing.medicinesauthority@gov.mt](mailto:postlicensing.medicinesauthority@gov.mt)

▼ Quinsair 240 mg nebuliser solution is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

## Company contact point

Should you have any questions or require additional information, please call Medical Information at:

Company	Product name	Email	Phone
Actavis Group PTC ehf	Levoxa 250mg film-coated Tablets Levoxa 500mg film-coated Tablets Levofloxacin Solution for Infusion 5mg/ml Siprox 250mg film coated tablets Siprox 500mg film coated tablets	PHVMALTA@actavis.com	+30 211 880 5166
Bayer plc	Ciproxin 250mg Film-coated Tablets Ciproxin 500mg Film-coated Tablets Ciproxin Solution for Infusion 100mg/50ml Ciproxin Solution for Infusion 200mg/100ml Avelox 400mg film-coated Tablets Avelox 400mg/250ml solution for infusion	pv@alfredgera.com	+ 356 21446205
Beximco Pharmaceuticals Ltd	Levofloxacin Beximco Coated Tablets 250mg Levofloxacin Beximco Coated Tablets 500mg	rea@bpl.net	+880 2 58611001 ext 20057
BIAL – Portela & C <sup>a</sup> , S.A.	UROFLOX, 400mg, film-coated Tablets	kzammit@adc.com.mt	+356 22778116
Chiesi Farmaceutici S.p.A.	Quinsair 240 mg nebuliser solution	GlobalPV@chiesi.com	+39 0521 279701 +39 0521 1689412
Clarix Lifesciences UK Limited	Ciprofloxacin 2mg/ml Solution for Infusion	medinfo@peckforton.com summerfield@riemser.com	+44 (0)1628 771800
Clonmel Healthcare Limited	Profloxin Tablet, film coated 250mg Profloxin Tablet, film coated 500mg	medicalinformation@clonmel-health.ie	+353 52 6177777
COOPER S.A. Pharmaceuticals	Nafloxin Injectable Solution for Infusion 200mg/100ml Levofloxacin Cooper 500mg/100ml solution for I.V. infusion	achristopoulou@zeincro.com safety@zeincro.com	+30 2108045712
Delorbis Pharmaceuticals Ltd	Viprolox 250mg Film coated tablets Viprolox 500mg Film-coated tablets FloxaVal 500mg Film-coated tablets	delorbis@delorbispharma.eu	+357 22 845 000
Europharma Ltd	Amesol 500mg Film-Coated Tablets	alex.fenech@europharma.com.mt	+356 2385 9239
Fresenius Kabi Italia S.r.l.	Ciprofloxacin Kabi 200mg/100ml solution for infusion Levofloxacin Solution for Infusion 5mg/ml	farmacovigilanza@fki-srl.legalmail.it	+39 0456649402 +39 3489710480
Ibigen S.r.L	Ciprofloxacin Ibigen 100mg/50ml solution for infusion Ciprofloxacin Ibigen 200mg/100ml solution for infusion Ciprofloxacin Ibigen 400mg/200ml solution for infusion Levofloxacin Ibigen Solution for Infusion 5mg/ml (50ml vial) Levofloxacin Ibigen Solution for Infusion 5mg/ml (100ml vial)	abusuttill@drugsalesltd.com	+356 21419070 +356 21419071 +356 21419072

Company	Product name	Email	Phone
KRKA, d. d., Novo Mesto	Ciprinol 250mg film-coated Tablets Ciprinol 500mg film-coated Tablets	pharmacovigilance@krka.biz	+386 14751100
Medical Logistics Ltd.	Ciprofloxacin 250mg Film-coated tablet Ciprofloxacin 500mg Film-coated tablet	samantha@ml.com.mt	+356 27559990
Medicem Limited	Ciproxin Tablet, film coated 500mg	crouchermartin@gmail.com alansammur@gmail.com	+356 99471241 +356 99422232
Neofarma Pharmaceuticals Ltd	Tavanic Coated Tablets 500mg	info@neofarma.com.mt	+356 20109494 +356 99109494
Noridem Enterprises Ltd.	Levofloxacin Solution for Infusion 5mg/ml Ciprofloxacin Solution for Infusion 2mg/ml	pv@demo.gr	+30 2108161802
Norma Hellas S.A	Revionorm Solution for Infusion 200mg/100m	safety@pharmassist.gr merkouri@pharmassist.gr	+30 2106561435
P and D Pharmaceuticals Limited	Cipro Inj 2mg/ml 50m	info@pdpharm.co.uk	+44 1420487501 - 207
PIAM Farmaceutici S.p.A.	TRISSIL 500 mg film-coated tablets	terrire@piamfarmaceutici.com piam@gbpharmaservices.it	+39 010 518621
Remedica Limited	Trizolin 400 mg Film-coated tablets Zindolin 250 mg Film-coated tablets	a.vasiliou@remedica.com.cy	+357 25553251
Rowex Ltd	Cifox Tablet, film coated 250mg Cifox Tablet, film coated 500mg Cifox Tablet, film coated 750mg	pv@rowa-pharma.ie	+353 (0)2750077
Sanofi Malta Ltd	Tavanic 500 mg film-coated tablets	Graziella.gravino@sanofi.com	+356 21493022
S.C. AC Helcor S.R.L.	Ciprolen 250 mg	office@achelcor.ro	+40362-401206
	Ciprolen 500 mg		
TAD Pharma GmbH	Norflosal	drug-safety@tad.de	+49 (0)47216060
Villerton Invest S.A.	Ciprofloxacin 2mg/ml solution for infusion	abusutil@drugsalesltd.com	+356 21419070 +356 21419071 +356 21419072

Yours faithfully,

**Post-Licensing Directorate  
Medicines Authority**

**Disclaimer**

*This Direct Healthcare Professional Communication has been submitted to you on behalf of Actavis Group PTC ehf, Bayer plc, Beximco Pharmaceuticals Ltd, BIAL – Portela & C, S.A., Chiesi Farmaceutici S.p.A., Claris Lifesciences UK Limited, Clonmel Healthcare Limited, COOPER S.A. Pharmaceuticals, Delorbis Pharmaceuticals Ltd, Europharma Ltd, Fresenius Kabi Italia S.r.l., Ibigen S.r.l., KRKA, d. d., Novo Mesto, Medical Logistics Ltd., Medicem Limited, Neofarma Pharmaceuticals Ltd, Noridem Enterprises Ltd., Norma Hellas S.A, P and D Pharmaceuticals Limited, PIAM Farmaceutici S.p.A., Remedica Limited, Rowex Ltd, Sanofi Malta Ltd, S.C. AC Helcor S.R.L., TAD Pharma GmbH, Villerton Invest S.A.*