Direct Healthcare Professional Communication

Systemic and inhaled quinolone and fluoroquinolone antibiotics – risk of disabling, long-lasting and potentially irreversible side effects and restrictions on use

March 2019

Dear Healthcare professional,

Marketing authorisation holders of quinolone and fluoroquinolone antibiotics products in agreement with the European Medicines Agency (EMA) and the Health Products Regulatory Authority, would like to inform you on 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 pipemidic 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 has been also recently updated to include the risk of aortic aneurysm and dissection. See relevant information on HPRA website:

https://www.hpra.ie/docs/default-source/default-document-library/important-safety-information---systemic-and-inhaled-fluoroquinolones.pdf

Further information

For more details, please refer to EMA review at:
https://www.ema.europa.eu/en/medicines/human/referrals/quinolone-fluoroquinolone-containing-medicinal-products and to the updated product information at www.HPRA.ie

Call for reporting

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system:

- Online Reporting via the HPRA Website: www.hpra.ie
- Using downloadable form from the HPRA website. An adverse reaction report form can be downloaded from the HPRA website. This can be sent by Freepost to the HPRA or by email to medsafety@hpra.ie
- By telephoning the Pharmacovigilance Section of the HPRA, (01) 676 4971

Company contact point

Suspected adverse reactions should also be reported to the relevant Marketing Authorisation Holders (see contact details below). This information is being provided jointly by the following MAHs:

Marketing Authorisation Holder	**Product Name**	**E-mail**	**Phone**	**Fax**
Accord Healthcare Limited	Ciplox 250 mg Film-coated Tablets Ciplox 500 mg Film-coated Tablets Ciplox 750 mg Film-coated Tablets	medinfo@accord-healthcare.com RegulatoryAffairsIreland@accord-healthcare.com	+44 (0) 1271 385 257	Non applicable
Bayer Limited	Avelox 400 mg film-coated tablets Avelox 400 mg/250 ml solution for infusion Ciproxin 250 mg film-coated tablets Ciproxin 500 mg film-coated tablets Ciproxin 750 mg film-coated tablets Ciproxin Solution for Infusion 2 mg/ml, 100ml Ciproxin Solution for Infusion 2 mg/ml, 200ml	Info.ireland@bayerhealthcare.com	+353 1 2163300	+353 1 206 1456
Bluefish Pharmaceuticals	Levofloxacin Bluefish 250 mg film-coated tablets Levofloxacin Bluefish 500 mg film-coated tablets	drugreaction@bluefishpharma.com	0046 8 519116 00	0046 8 51911690
Chiesi Farmaceutici S.p.A.	QUINSAIR	GlobalPV@chiesi.com	Office: +39 0521 279 701	Fax: +39 0521 188 5003

Claris Lifesciences UK Limited	Ciprofloxacin 2mg/ml Solution for Infusion (non-PVC bags; vials; bottles) Levofloxacin 5 mg/ml Solution for Infusion	Primary: medinfo@peckforton.com Secondary: summerfield@riemser.com	+44 (0)1628 771800;	Non applicable
Clonmel Healthcare Ltd	PROFLOXIN 250 MG FILM-COATED TABLETS PROFLOXIN 500 MG FILM-COATED TABLETS	medicalinformation@clonmel-health.ie	+353 52 617777 7	+353 52 6177791
Fannin Limited	Truoxin 250mg Film-coated Tablets Truoxin 500mg Film-coated Tablets	medical@dccvital.com	+353 (0)90 666 1109	+353 (0)90 666 1921
Fresenius Kabi Ltd	Levofloxacin 5mg/ml solution for infusion Moxifloxacin 400 mg/250 ml solution for infusion	Pharmacovigilance.GB@fresenius-kabi.com	+44 (0)1928 533 612	+44 (0)1928 533 587
Hikma Farmacêutica (Portugal), S.A.	Truoxin I.V. 400 mg/200 ml solution for infusion Truoxin I.V. 200 mg/100 ml solution for infusion Levofloxacin 5 mg/ml solution for infusion	Portugaleupharmacovigilance@hikma.com	+351 210 438 540	+351 219 615 102
Hospira UK Limited	Ciprofloxacin 2 mg/ml solution for infusion	GBR.AEReporting@Pfizer.com	1800 633 363	Non applicable

Krka, d.d. Novo mesto	Ciprofloxacin Krka Levofloxacin Krka	Pharmacovigilance.ie@krka.biz	01-2939180	Non applicable
McDermott Laboratories Ltd t/a Gerard Laboratories	Cifloxager 250 mg Film-coated Tablets Cifloxager 500 mg Film-coated Tablets Ciprofloxacin 2mg/ml solution for Infusion Tavager 500 mg film-coated tablets	info.uk@mylan.co.uk	+44 (0) 174 882 8888	Non applicable
Noridem Enterprises Ltd.	Ciprofloxacin 2 mg/ml Solution for Infusion Levofloxacin 5 mg/ml solution for infusion	pv@demo.gr	+30 210 8161802	+ 30 210 81 61 587
Rowex Ltd.	Cifox 250mg, 500mg & 750mg Film-coated tablets	pv@rowa-pharma.ie	+3532 750077	+353275 0417
Sanofi-Aventis Ireland Ltd. T/A SANOFI	Tavanic (levofloxacin hemihydrate) 5 mg/ml solution for infusion (PA: 540/77/001) Tavanic (levofloxacin hemihydrate) 250 mg film-coated tablets (PA: 540/77/002) Tavanic (levofloxacin hemihydrate) 500 mg film-coated tablets (PA: 540/77/003)	Pharmacovigilance contact: IEPharmacovigilance@sanofi.com Medical Information contact: IEmedinfo@sanofi.com	+353 1 403 5600	+353 1 403 5601

	Tarivid (ofloxacin hydrochloride) IV 2 mg/ml Solution for Infusion (PA: 540/76/002) Tarivid (ofloxacin) 200 mg Film-Coated Tablets (PA: 540/76/003)			
Teva Pharma B.V.	Ciprofloxacin Teva 250 mg Film-coated Tablets Ciprofloxacin Teva 500 mg Film-coated Tablets	medinfo@tevauk.com	+44 (0)20 7540 7117	+44 (0)20 7540 7349

Yours sincerely,

TRISTAN COOPER
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Tristan Cooper
Medical Director
Bayer Limited
22nd March 2019

On behalf of the following Marketing Authorisation Holders:

Accord Healthcare Ireland Ltd.
Bayer Limited
Bluefish Pharmaceuticals
Chiesi Farmaceutici S.p.A.
Claris Lifesciences UK Limited
Clonmel Healthcare Ltd
Fannin Limited
Fresenius Kabi, UK Ltd
Hikma Farmacêutica (Portugal), S.A.
Hospira UK Limited
KrKa, d.d. Novo mesto
McDermott Laboratories Ltd t/a Gerard Laboratories
Noridem Enterprises Ltd.
Rowex Ltd.
Sanofi-Aventis Ireland Ltd. T/A SANOFI
Teva Pharma B.V.