March 2020

Direct Healthcare Professional Communication

Systemic and inhaled quinolone and Fluoroquinolone antibiotics – risk of disabling, long-lasting and potentially irreversible side effects

Dear Healthcare Professional,

Following a European safety review, Mercury Pharmaceuticals Limited in agreement with the MHRA and the European Medicines Agency (EMA), would like to inform you of the following safety information (initially published by EMA in March 2019).

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 have been reviewed.

• Do **not** prescribe any quinolone and fluoroquinolone antibiotic for:
  - o non-severe or self-limiting infections, or non-bacterial conditions
  - o particular types of mild to moderate infections* unless other antibiotics that are commonly recommended for these infections are considered inappropriate (such as acute exacerbation of chronic bronchitis and chronic obstructive pulmonary disease (COPD))

• Avoid use in patients who have previously had serious adverse reactions with a quinolone or fluoroquinolone antibiotic.

• Ciprofloxacin or levofloxacin should not be prescribed for uncomplicated cystitis unless other antibiotics that are commonly recommended are considered inappropriate.

• Exercise special caution when prescribing these medicines for the elderly, patients with renal impairment, patients with solid organ transplants, and patients concurrently treated with corticosteroids, since 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.

*Please refer to the product-specific Summary of Product Characteristics for ciprofloxacin, levofloxacin, moxifloxacin and ofloxacin for the full updated indications and precautions/warnings.

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Background on the 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 under-reporting can be assumed. Due to the seriousness of these reactions in previously healthy people, 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 all fluoroquinolone-containing medicines have been updated with this information.

(The product information of fluoroquinolones has been also updated to include the risk of aortic aneurysm and dissection. See relevant information on https://www.gov.uk/drug-safety-update/systemic-and-inhaled-fluoroquinolones-small-increased-risk-of-aortic-aneurysm-and-dissection-advice-for-prescribing-in-high-risk-patients)

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 http://www.mhra.gov.uk/spc-pil/

Call for reporting

Healthcare professionals should report suspected adverse drug reactions (ADRs) in patients taking quinolone or fluoroquinolone antibiotics using the Yellow Card website or via the Yellow Card app. When reporting, please provide as much information as possible.

Download the app today via iTunes Yellow Card for iOS devices or via Play Store Yellow Card for Android devices.

Alternatively, report ADRs via the Yellow Card website - https://yellowcard.mhra.gov.uk/ or on prepaid Yellow Cards available by writing to FREEPOST YELLOW CARD (no other address details necessary); by emailing yellowcard@mhra.gov.uk ; at the back of the British National Formulary (BNF); by telephoning the Commission on Human Medicines (CHM) free phone line: 0800-731-6789; or by downloading and printing a form from the Yellow Card section of the MHRA website.

You can also report adverse events to Mercury Pharmaceuticals Limited at:

Company name	E-mail	Telephone number	Fax Number
Mercury Pharmaceuticals Limited	medicalinformation@advanzpharma.com	+44 (0) 8700 70 30 33	+ 44 (0) 20 8588 9200

Company contact point

Company name	Name of contact person	Contact Details
Mercury Pharmaceuticals Limited	Dr. Anju Agarwal, Head of Drug Safety	E-mail: anju.agarwal@advanzpharma.com Telephone Number: +44 208 588 9225

Signed By:

Anju Agarwal. 19/Mar/2020.

Dr. Anju Agarwal

Head of Drug Safety

Mercury Pharmaceuticals Limited (ADVANZ PHARMA GROUP)