# Study of impact of EU label changes for fluoroquinolone containing medicinal products for systemic and inhalation use - post-referral prescribing trends

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#### Administrative details

#### **PURI**

https://redirect.ema.europa.eu/resource/48010

#### **EU PAS number**

**EUPAS37856** 

#### Study ID

48010

#### **DARWIN EU® study**

No

#### Study countries

Belgium

France

Germany

Netherlands

Spain

**United Kingdom** 

#### Study description

In November 2018 a referral procedure (EMA/H/A-31/1452) under Article 31 of Directive 2001/83/EC resulting from pharmacovigilance data concluded that serious adverse

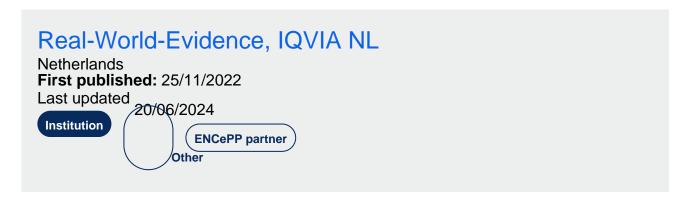
reactions including tendon, muscle and joint disorders, neurologic and psychiatric disorders listed in the product information of different (fluoro)quinolones could in rare cases become long-lasting, disabling and potentially even irreversible and substantially disrupt patients' daily activities. To maintain a favourable benefit-risk balance for all (fluoro)quinolone containing medicinal products for systemic use, revised indications, warnings, and other changes to the product information, including direct healthcare professional communication (DHPC) were implemented in EU Member States including recommendations for cessation of prescribing for milder, non-severe or self-limiting infections, and restrictions for other indications. The study objectives are: 1.To determine the drug utilisation and prescription patterns of fluoroguinolone containing medicinal products over the period 2016 and 2020 by a)estimating monthly incident drug use, stratified by on label indications and off label indications. b)Estimation of early discontinuation proportion 2. To evaluate the impact of regulatory interventions on fluoroquinolone prescribing patterns using time series analysis. 3. To determine prescribers' compliance with warnings as described in fluoroguinolones SmPC section 4.4, in particular on tendinitis and tendon rupture as well as on aortic aneurysm/dissection 4. To determine monthly incident prescription rates for alternative antibiotics prescribed in patients where systemic or inhalation use fluoroguinolones have previously been prescribed and discontinued. Data from six European countries namely IPCI (the Netherlands), SIDIAP (Catalonia Spain) and IQVIA (UK IMRD, LPD Belgium, DA Germany and LPD France). Data from these databases have been mapped to the OMOP Common Data Model.

#### Study status

Finalised

#### Research institution and networks

#### Institutions



Multiple centres: 6 centres are involved in the study

### Contact details

#### Study institution contact

**Deborah Layton** 

Study contact

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**Primary lead investigator** 

**Deborah Layton** 

Primary lead investigator

# Study timelines

#### Date when funding contract was signed

Actual:

06/05/2020

#### Study start date

Actual:

01/01/2016

#### Date of final study report

Planned:

01/06/2022

Actual:

01/07/2022

# Sources of funding

EMA

# Study protocol

Fluroquinolone - Study Protocol.pdf(821.88 KB)

# Regulatory

Was the study required by a regulatory body?

Yes

# Is the study required by a Risk Management Plan (RMP)? Not applicable

# Methodological aspects

# Study type list

#### Study topic:

Human medicinal product

#### Study type:

Non-interventional study

#### Scope of the study:

Drug utilisation

#### Data collection methods:

Secondary data collection

#### Main study objective:

The overall aim of this study is to evaluate the impact of the regulatory actions taken for fluoroquinolone containing medicinal products following the 2018 referral procedure, using healthcare databases of six European countries.

# Study Design

Non-interventional study design

Cohort

# Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

10000096303 ofloxacin 10000096304 ciprofloxacin 100000096308 norfloxacin 10000096309 lomefloxacin 10000096314 levofloxacin 100000096316 moxifloxacin

# Population studied

#### Short description of the study population

The study population in each database will include all patients who contribute observation person-time at risk in each database during the study time period and meet the study selection criteria.

In each country, patients who meet all of the inclusion criteria and none of the exclusion criteria will be selected.

Inclusion Criteria

The inclusion criteria are:

- All patients with an active registration status during the study time period
- Continuous enrolment in the database for more than 12 months

Exclusion Criteria
Patients will be excluded if they are

Missing age or sex

#### Age groups

Preterm newborn infants (0 – 27 days)

Term newborn infants (0 - 27 days)

Infants and toddlers (28 days – 23 months)

Children (2 to < 12 years)

Adolescents (12 to < 18 years)

Adults (18 to < 46 years)

Adults (46 to < 65 years)

Adults (65 to < 75 years)

Adults (75 to < 85 years)

Adults (85 years and over)

#### Estimated number of subjects

800000

# Study design details

#### Data analysis plan

This is a drug utilization study with a time series analysis component to identify the potential impact of regulatory interventions on fluoroquinolones prescribing trends. An initial exploratory descriptive analysis will be conducted for each database-specific cohort. Crude and stratified incidence of drug use, drug discontinuation and use of alternative treatment use will be calculated. A Joinpoint regression model will be used to investigate changes in prescribing patterns over calendar time. Prescriber compliance with labelled warnings for use mentioned in the product information will be investigated, as well as, using incidence of drug use across indications and risk factors.

#### **Documents**

#### Study results

Final\_Report\_Fluoro.pdf(8.67 MB)

# Data management

#### Data sources

#### Data source(s), other

SIDIAP, IPCI, IMS LifeLink:Longitudinal Prescription Data (LRx) - Belgium, MS LifeLink Longitudinal Prescription Data - France, IQVIA Disease Analyzer Germany

#### Data sources (types)

Electronic healthcare records (EHR)

# Use of a Common Data Model (CDM)

#### **CDM** mapping

No

# Data quality specifications

#### **Check conformance**

Unknown

#### **Check completeness**

Unknown

# **Check stability** Unknown

Check logical consistency Unknown

# Data characterisation

**Data characterisation conducted** No