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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Study Finalised

Administrative details

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 fluoroquinolone 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 fluoroquinolones 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 fluoroquinolones 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 institutions and networks

Institutions

IQVIA NL, Real-World-Evidence

Netherlands

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Institution **Other** **ENCePP partner**

Multiple centres: 6 centres are involved in the study

Contact details

Study institution contact

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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

Study type list

Study topic:

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Drug utilisation

Data collection methods:

Secondary use of data

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

(J01MA01) ofloxacin

ofloxacin

(J01MA02) ciprofloxacin

ciprofloxacin

(J01MA06) norfloxacin

norfloxacin

(J01MA07) lomefloxacin

lomefloxacin

(J01MA12) levofloxacin

levofloxacin

(J01MA14) moxifloxacin

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

ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

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