A post-authorisation safety study (PASS) to evaluate the long-term cardiovascular and psychiatric safety profile of methylphenidate (MPH) in adult patients with attention deficit/hyperactivity disorder (ADHD) in European Countries (PASS on methylphenidate in adults)

First published: 04/03/2021

Last updated: 22/07/2024

Study Planned

Administrative details

PURI

https://redirect.ema.europa.eu/resource/47509

EU PAS number

EUPAS39745

Study ID

47509

DARWIN EU® study

No

Study countries

- ☐ Denmark
- ☐ Norway
- ☐ Sweden

Study description

There is limited and inconsistent data from pharmacoepidemiologic studies on MPH use and adverse cardiovascular or psychiatric events, especially among adults. The overall aim of the PASS is to compare the risk of first-time cardiovascular or psychiatric events in association with new use of MPH monotherapy versus new use of non-MPH ADHD medications (lisdexamfetamine, dexamfetamine and atomoxetine, monotherapy) and versus no use of ADHD medication in adult patients aged ≥18 years newly diagnosed with ADHD, in healthcare databases of three European countries

Study status

Planned

Research institutions and networks

Institutions

IQVIA

☐ United Kingdom

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Institution | Non-Pharmaceutical company | ENCePP partner

Contact details

Study institution contact

Sofia Correia

Study contact

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Primary lead investigator

Sofia Correia

Primary lead investigator

Study timelines

Date when funding contract was signed

Actual: 27/09/2018

Study start date

Planned: 31/03/2021

Data analysis start date

Planned: 01/10/2021

Date of interim report, if expected

Planned: 30/06/2022

Date of final study report
Planned: 30/06/2024

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Medice

Regulatory

Was the study required by a regulatory body?

Yes

Is the study required by a Risk Management Plan (RMP)?

EU RMP category 1 (imposed as condition of marketing authorisation)

Regulatory procedure number

EMEA/H/N/PSP/S/0064

Methodological aspects

Study type

Study type list

Study type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Main study objective:

To compare the incidence rate of first-time cardiovascular events (composite) in adults newly diagnosed with ADHD between cumulative person-time newly exposed to MPH versus cumulative person-time newly exposed to MPH versus cumulative person-time newly treated with non-MPH ADHD medication.

Study Design

Non-interventional study design

Cohort

Other

Non-interventional study design, other

Retrospective cohort study (new user design)

Study drug and medical condition

Study drug International non-proprietary name (INN) or common name

ATOMOXETINE

METHYLPHENIDATE

Anatomical Therapeutic Chemical (ATC) code

(N06BA02) dexamfetamine

dexamfetamine

(N06BA04) methylphenidate

methylphenidate

(N06BA09) atomoxetine

atomoxetine

(N06BA12) lisdexamfetamine

lisdexamfetamine

Medical condition to be studied

Attention deficit hyperactivity disorder

Population studied

Age groups

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

500000

Study design details

Outcomes

First-time cardiovascular events (composite of hospitalization for myocardial infarction, cardiomyopathy, left-ventricular hypertrophy, hospitalization for stroke, ventricular arrhythmia, sudden cardiac death or all other causes of cardiovascular death of interest), first-time psychiatric events of interest (composite of psychotic or manic symptoms, suicidal ideation or behaviour, aggressive and hostile behaviour, anxiety or agitation or tension, depressive symptoms, motor or verbal tics)

Data analysis plan

• Descriptive analysis for each cohort post data-extraction,

• Cohort-specific descriptive statistics summarizing demographic, health and clinical patient characteristics will be presented.

• Crude incidence (presented as both proportions and rates) for the relevant outcomes reported during person-time treated with MPH, treated with Non-MPH, or time untreated will be calculated for 1-year, 2-year, 3-year, 4-year and 5-year intervals cumulatively, stratified by potential confounders

• Time to event, high and low risk periods will be summarized.

• Univariate analyses will be used to inform on potential confounders and risk factors.

• Cardiovascular and psychiatric risk scores will be determined via regression

• Time-varying analysis of cardiovascular and psychiatric hazard rates will be performed using time-varying Cox regression models by country and pooled estimate calculated using random effects meta-analysis.

Data management

Data sources

Data source(s)

Danish registries (access/analysis)

Sweden National Prescribed Drugs Register / Läkemedelsregistret

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Data source(s), other

Norwegian Prescription Database (NorPD)

Data sources (types)

Administrative healthcare records (e.g., claims)

Disease registry

Electronic healthcare records (EHR)

Other

Data sources (types), other

Exposure registry

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