Comparative cardiovascular side effects of medications for attention-deficit/hyperactivity disorder: protocol of a case non-case study based on the WHO international pharmacovigilance database

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Study Planned

Administrative details

EU PAS number

EUPAS47582

Study ID

47583

DARWIN EU® study

No

Study countries

☐ France

Study description

Treatment for individuals with ADHD includes both non-pharmacological and pharmacological strategies. Medications approved by the U.S. Food and Drug Administration (FDA) include stimulants (amphetamines and methylphenidate) and non-stimulants (atomoxetine, clonidine, guanfacine extended release, and viloxazine). In the past few decades, prescriptions for ADHD drugs have increased significantly across many countries. Overall, these medications are effective and generally well tolerated, although their use may be associated with adverse effects, in particular decreased appetite, decreased height and weight gain, sleep disturbances, tics, seizures, psychotic symptoms, and increased blood pressure and heart rate. To our knowledge, no study has been carried out using VigiBase® to compare ADHD drugs in terms of the risk of reporting cardiovascular adverse effects. Here, we present the protocol of a study aimed at comparing the risk of reporting cardiovascular events among 12 medications used to treat ADHD, individually and grouped according to their major pharmacological classes.

Study status

Planned

Research institutions and networks

Institutions

Toulouse University Hospital

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Institution

Pharmacologie En Population cohorteS et biobanqueS

Contact details

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Primary lead investigator

Pierjan Fourniols

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 02/05/2022

Study start date

Planned: 30/05/2022

Data analysis start date

Planned: 02/06/2022

Date of final study report
Planned: 21/06/2022

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Toulouse University Hospital

Regulatory

Was the study required by a regulatory body?

No

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

Not applicable

Methodological aspects

Study type

Study type list

Study type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Disease epidemiology

Drug utilisation

Main study objective:

The main objective : comparing the risk of reporting cardiovascular events among 12 medications used to treat ADHD, individually and grouped according to their major pharmacological classes.

Study Design

Non-interventional study design

Other

Non-interventional study design, other

Case non-case study

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(N06BA07) modafinil

modafinil

(N06BA03) metamfetamine

metamfetamine

(N06BA09) atomoxetine

atomoxetine

(N06BA02) dexamfetamine

dexamfetamine

(N06BA01) amfetamine

amfetamine

(A08AA62) bupropion and naltrexone

bupropion and naltrexone

(N06BA04) methylphenidate

methylphenidate

(C02AC02) guanfacine

guanfacine

(C02AC01) clonidine

clonidine

(N06BA11) dexmethylphenidate

dexmethylphenidate

Medical condition to be studied

Cardiac disorder

Additional medical condition(s)

Hypertension Cardiac Arrythmias,Torsade de pointes/QT prolongation,Heart failure,Ischemic heart disease,Central nervous system haemorrhages and cerebrovascular conditions,Cardiac valve disorders,Myocardial disorders

Population studied

Age groups

- 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

10000

Study design details

Outcomes

Risk of reporting cardiovascular events among : 1. Hypertension 2. Cardiac Arrythmias 3. Torsade de pointes/QT prolongation 4. Heart failure 5. Ischemic heart disease 6. Central nervous system haemorrhages and cerebrovascular conditions 7. Central nervous system haemorrhages and cerebrovascular conditions 8. Myocardial disorders

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Data analysis plan

This is a disproportionality analyses using Vigibase®, the World Health Organization's global database of Individual Case Safety Reports (ICSRs), which has included more than 30 million reports since 1967 (as of May 2022) from over 130 countries. The WHO Uppsala Monitoring Center stores these ICSRs, which are spontaneous reports of adverse drug reactions from a suspected causative agent, as reported by health professionals, consumers, or drug manufacturers. Vigibase® includes information on the patient's age, gender, medical history, and country, as well as on the medications taken, with their start and end dates. Reports are categorized according to the seriousness of

the adverse drug reaction. The Medical Dictionary for Regulatory Activities (MedDRA) is used to code adverse effects

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

WHO international pharmacovigilance database France

Data sources (types)

Spontaneous reports of suspected adverse drug reactions

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