

# Cohort Study of the Incidence of Major Cardiovascular Events in New Adult Users of Lisdexamfetamine and Remote Adult Users of Other ADHD Treatments

**First published:** 05/09/2017

**Last updated:** 02/07/2024

Study

Finalised

## Administrative details

### EU PAS number

EUPAS20546

### Study ID

43216

### DARWIN EU® study

No

### Study countries

☐ Denmark

☐ Sweden

## Study description

This study will consist of multiple observational (non-interventional) population-based cohort studies of patients initiating Lisdexamfetamine dimesylate (LDX) compared with patients with remote use of other attention deficit and hyperactivity disorder (ADHD) medications, in three electronic health care data sources: the Danish National Registries, and the Swedish National Registers. The main objective of this study is to estimate the incidence rate (IR) and the adjusted incidence rate ratios (IRRs) of the composite major adverse cardiovascular events (MACE) endpoint in a cohort of adult patients who are current new users of LDX compared with a cohort of remote users of other ADHD treatments. Current use for LDX new users is defined as the duration of the LDX prescription or dispensing plus 30 days. The remote use of other ADHD treatments will be generated by selecting adult patients with at least one prescription/dispensing for a medication indicated for ADHD, other than LDX, during the 24 months prior to the index date and with no prescriptions or dispensings of these medications in at least the last 180 days before index date. The analysis will be conducted separately in each data source, and overall estimates of effect will be obtained using meta-analytic techniques as appropriate. The primary endpoint, MACE, will comprise the first occurrence of any of its individual components during follow-up: hospitalisation for acute myocardial infarction, fatal or non-fatal, hospitalisation for stroke, fatal or non-fatal, out-of-hospital coronary heart disease death, and out-of-hospital cerebrovascular death. Secondary endpoints are an extended MACE (EMACE) endpoint that includes hospitalisation for either unstable angina or TIA, the composite coronary and stroke components of EMACE, and an additional secondary endpoint that will be a composite of sudden cardiac death and serious ventricular arrhythmias.

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## Study status

Finalised

## Research institutions and networks

## Institutions

### RTI Health Solutions (RTI-HS)

- ☐ France
- ☐ Spain
- ☐ Sweden
- ☐ United Kingdom
- ☐ United Kingdom (Northern Ireland)
- ☐ United States

**First published:** 21/04/2010

**Last updated:** 13/03/2025

**Institution**

Not-for-profit

ENCEPP partner

### Centre for Pharmacoepidemiology, Karolinska Institutet (CPE-KI)

- ☐ Sweden

**First published:** 24/03/2010

**Last updated:** 23/04/2024

**Institution**

Educational Institution

Laboratory/Research/Testing facility

Not-for-profit

ENCEPP partner

### RTI Health Solutions (RTI-HS)

- ☐ France

- ☐ Spain
- ☐ Sweden
- ☐ United Kingdom
- ☐ United Kingdom (Northern Ireland)
- ☐ United States

**First published:** 21/04/2010

**Last updated:** 13/03/2025

**Institution**

**Not-for-profit**

**ENCEPP partner**

## Contact details

### Study institution contact

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**Study contact**

[crebordosa@rti.org](mailto:crebordosa@rti.org)

### Primary lead investigator

Cristina Rebordosa

**Primary lead investigator**

## Study timelines

### Date when funding contract was signed

Planned: 01/06/2017

Actual: 01/06/2017

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**Study start date**

Planned: 01/12/2019

Actual: 30/09/2019

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**Date of final study report**

Planned: 30/06/2020

Actual: 18/12/2020

## Sources of funding

- Pharmaceutical company and other private sector

## More details on funding

Shire Human Genetic Therapies, Inc., a wholly owned subsidiary of the Takeda Pharmaceutical Company Limited

## Study protocol

[0304010 - LDX Protocol Final Version \(v2.0\)- 08March2016\\_redacted.pdf](#)(6.91 MB)

[LDX protocol\\_final version 3.0\\_final\\_3Jun2019\\_Redacted.pdf](#)(2.29 MB)

## Regulatory

**Was the study required by a regulatory body?**

Yes

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

EU RMP category 2 (specific obligation of marketing authorisation)

## Methodological aspects

**Study topic:**

Disease /health condition  
Human medicinal product

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**Study type:**

Non-interventional study

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**Scope of the study:**

Assessment of risk minimisation measure implementation or effectiveness

**Data collection methods:**

Secondary use of data

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**Main study objective:**

The primary objective of this study is to estimate, in real-world settings, the incidence rate (IR) and the adjusted incidence rate ratios (IRRs) of the composite major adverse cardiovascular events (MACE) endpoint in a cohort of adult patients who are current new users of LDX compared with a cohort of remote users of other ADHD treatments in three European data sources.

## Study Design

**Non-interventional study design**

Cohort

## Study drug and medical condition

**Anatomical Therapeutic Chemical (ATC) code**

(N06BA12) lisdexamfetamine

lisdexamfetamine

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**Additional medical condition(s)**

Major Cardiovascular Events (MACE)

## Population studied

**Short description of the study population**

The source population will be all individuals aged 18 years or older registered in the study databases from the date LDX will become available for the treatment of ADHD in adults in each country until the end of study period. To be eligible for inclusion into the study population, individuals should have at least 12 months of data available prior to cohort entry. The study will include two cohorts identified from all eligible individuals in the study data sources: the LDX cohort and the remote use of other ADHD treatments cohort.

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**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)

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**Estimated number of subjects**

170940

## Study design details

## Outcomes

Major cardiovascular events (MACE). MACE, will comprise hospitalisation for acute myocardial infarction (AMI), fatal or non-fatal, hospitalisation for stroke, fatal or non-fatal, out-of-hospital coronary heart disease death, and out-of-hospital cerebrovascular death. Extended MACE (EMACE). EMACE comprises all MACE components plus hospitalisation for either unstable angina or transient ischaemic attack (TIA), the composite coronary and stroke components of EMACE, and a composite of sudden cardiac death and serious ventricular arrhythmias.

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## Data analysis plan

Each research partner will conduct country-specific analyses within each data source to (1) select the study population, (2) describe the study cohorts, including patterns of demographics, medical history, exposures, and endpoints, (3) within its data, estimate exposure propensity scores that will be used to control for confounding, (4) create a summary of aggregated data set based on counts of patients, person-years, and outcome events according to the strata of age, sex and propensity scores, (5) analyse IR and standardised IRs, and (6) analyse crude and adjusted IRRs. IRs will be standardised to the distribution of person-time of LDX users by age, sex, quintiles of the propensity score, and data source. The coordinating centre activities include conducting a (1) pooled description analysis of study cohorts, (2) pooled analysis of IR and standardised IRs, and (3) pooled analysis of crude and adjusted IRRs. Mantel-Haenszel methods will be used to summarise IRRs across strata.

## Documents

### Study results

[4765\\_Elvanse PASS\\_exec summary\\_FINAL\\_18Dec2020\\_Redacted.pdf](#)(173.25 KB)

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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)

Danish registries (access/analysis)

Sweden National Prescribed Drugs Register / Läkemedelsregistret

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### Data sources (types)

Disease registry

Drug dispensing/prescription data

Electronic healthcare records (EHR)

Other

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### Data sources (types), other

Hospital discharge data

## Use of a Common Data Model (CDM)

### CDM mapping

No

## Data quality specifications

**Check conformance**

Unknown

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**Check completeness**

Unknown

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**Check stability**

Unknown

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**Check logical consistency**

Unknown

## Data characterisation

**Data characterisation conducted**

No