DARWIN EU® - Assessing the potential association between venlafaxine and heart failure in adults

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Study Ongoing

Administrative details

EU PAS number

EUPAS1000000974

Study ID

1000000974

DARWIN EU® study

Yes

Study countries

- [ ] Denmark
- [ ] Finland
- [ ] Spain
- [ ] Sweden

United Kingdom

Study description

Venlafaxine is a dual-acting serotonin and norepinephrine reuptake inhibitor (SNRI) indicated for the treatment of depression, prevention of relapse and prevention of recurrence of depression, anxiety or generalized anxiety disorder, social anxiety disorder, and panic disorder.

Venlafaxine has a dose-dependent pharmacodynamic profile. At lower doses it primarily inhibits serotonin reuptake, while at higher doses (≥150 mg/day), it additionally inhibits norepinephrine reuptake and exerts weak inhibitory effects on dopamine reuptake.

Several cardiovascular effects are already labelled in section 4.8 of the Summaries of product characteristics (SmPC) in Europe, e.g., tachycardia and hypertension, Torsade de pointes, ventricular tachycardia, ventricular fibrillation, prolonged QT, and stress cardiomyopathy (Takotsubo cardiomyopathy).

A published case series and spontaneously reported cases (e.g., EudraVigilance, Vigibase, company global pharmacovigilance safety database) suggest an association between venlafaxine and cardiotoxicity (heart failure, cardiomyopathy other than Takotsubo). An observational study using high-quality data from the DARWIN EU® network could add important further evidence to evaluate the potential association.

The European Medicines Agency (EMA) has therefore requested a study to estimate the association between venlafaxine and heart failure/cardiomyopathy, using mirtazapine, which is indicated for the treatment of depression, as active comparator.

Study status

Ongoing

Research institutions and networks

Institutions

Department of Medical Informatics - Health Data Science, Erasmus Medical Center (ErasmusMC)

- [ ] Netherlands

First published: 03/11/2022

Last updated: 02/05/2024

Institution | Educational Institution | ENCePP partner

Networks

Data Analysis and Real World Interrogation Network (DARWIN EU®)

- [ ] Belgium
- [ ] Croatia
- [ ] Denmark
- [ ] Estonia
- [ ] Finland
- [ ] France
- [ ] Germany
- [ ] Greece
- [ ] Hungary
- [ ] Italy
- [ ] Netherlands
- [ ] Norway

- [ ] Portugal
- [ ] Spain
- [ ] Sweden
- [ ] United Kingdom

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Network

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Annika Jodicke

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 02/12/2025

Actual: 02/12/2025

Study start date

Planned: 27/03/2026

Actual: 27/03/2026

Date of final study report
Planned: 26/06/2026

Sources of funding

- EMA

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

Study design:

New user cohort studies will be conducted using routinely collected health data from 6 data sources from 5 countries across Europe and in 4 European Union (EU) member states.

Main study objective:

1) To assess the risk of incident heart failure and incident cardiomyopathy between new users of venlafaxine vs. new users of mirtazapine.
2) To assess the risk of heart failure exacerbation between new users of venlafaxine vs. new users of mirtazapine who have been diagnosed with heart failure before treatment initiation.
3) To characterise both new venlafaxine and new mirtazapine users at the time of treatment start (in terms of demographics, pre-defined comorbidities/comedication/conditions of interest, and drug utilisation) for contextualisation of Objectives 1+2.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(N06AX16) venlafaxine

venlafaxine

Additional medical condition(s)

heart failure

Population studied

Short description of the study population

The study population will include all individuals with a recorded first prescription for venlafaxine or mirtazapine within the study period from 01/01/2010 up to the end of data availability who meet the eligibility criteria at study entry.

Age groups

- **Adult and elderly population (≥18 years)**
  - Adults (18 to < 65 years)
    - Adults (18 to < 46 years)
    - Adults (46 to < 65 years)
  - Elderly (≥ 65 years)
    - Adults (65 to < 75 years)
    - Adults (75 to < 85 years)
    - Adults (85 years and over)

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)

Danish Health Data Registries

BIFAP - Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público (Pharmacoepidemiological Research Database for Public Health Systems)

The Information System for Research in Primary Care (SIDIAP)

Health Impact - Swedish Population Evidence Enabling Data-linkage

Clinical Practice Research Datalink (CPRD) GOLD

Data source(s), other

FinOMOP-THL

Use of a Common Data Model (CDM)

CDM mapping

Yes

CDM Mappings

CDM name

OMOP

CDM website

https://www.ohdsi.org/Data-standardization/

CDM version

https://ohdsi.github.io/CommonDataModel/index.html

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

No