

# DARWIN EU® - Incidence of myoclonus in heart failure: a descriptive analysis in patients treated with sacubitril/valsartan and other treatments

**First published:** 30/10/2024

**Last updated:** 29/01/2025

Study

Ongoing

## Administrative details

### EU PAS number

EUPAS1000000351

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### Study ID

1000000351

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### DARWIN EU® study

Yes

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### Study countries

 Germany

 Spain

 United Kingdom

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## Study description

Sacubitril/valsartan (Entresto) is an angiotensin receptor-neprilysin inhibitor used to treat symptomatic chronic heart failure in both adults and children. Its dual mechanism of action involves inhibiting neprilysin and blocking the angiotensin II type-1 receptor, providing complementary cardiovascular benefits. The Pharmacovigilance Risk Assessment Committee (PRAC) is currently investigating a signal on a potential association between the use of sacubitril/valsartan and myoclonus.

Through this study, we aimed to investigate the incidence rate of myoclonus in the general population, newly diagnosed heart failure patients and patients with heart failure initiating sacubitril/valsartan, angiotensin-converting enzyme inhibitors (ACEi), and angiotensin receptor blockers (ARBs).

This study aims to estimate incidence rates of myoclonus in different populations of interest.

Specific study objectives:

1. To calculate the incidence rate of myoclonus in a newly diagnosed heart failure population and the general population, stratified by age groups and sex.
2. To calculate the incidence rate of myoclonus in a heart failure population following first initiation of treatment cohorts: sacubitril/valsartan, angiotensin-converting enzyme inhibitors (ACEi), and angiotensin receptor blockers (ARBs) (index date being the start of the treatment).

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## Study status

Ongoing

## Research institutions and networks

### Institutions

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

 Netherlands

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**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

**First published:** 01/02/2024

**Last updated:** 30/04/2025

Network

## Contact details

### Study institution contact

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Study contact

[study@darwin-eu.org](mailto:study@darwin-eu.org)

### Primary lead investigator

Julieta Politi

Primary lead investigator

## Study timelines

### Date when funding contract was signed

Planned: 23/09/2024

Actual: 23/09/2024

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### Study start date

Planned: 22/10/2024

Actual: 22/10/2024

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### **Date of final study report**

Planned: 06/01/2025

## Sources of funding

- EMA

## Study protocol

[DARWIN EU\\_Protocol\\_P3-C1-015\\_Sacubitril valsartan and risk of myoclonus V4.pdf](#) (831.26 KB)

## Regulatory

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

Yes

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

Not applicable

## Methodological aspects

### Study type

### Study type list

**Study topic:**

Human medicinal product

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**Study type:**

Non-interventional study

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**Scope of the study:**

Safety study (incl. comparative)

**Data collection methods:**

Secondary use of data

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**Study design:**

The incidence of the event of interest will be assessed using a population-level descriptive epidemiology design.

**Main study objective:**

1. To calculate the incidence rate of myoclonus in a newly diagnosed heart failure population and the general population, stratified by age groups and sex.
2. To calculate the incidence rate of myoclonus in a heart failure population following first initiation of treatment cohorts: sacubitril/valsartan, angiotensin-converting enzyme inhibitors (ACEi), and angiotensin receptor blockers (ARBs) (index date being the start of the treatment).

## Study Design

**Non-interventional study design**

Cohort

## Study drug and medical condition

**Medicinal product name**

ENTRESTO

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

SACUBITRIL

VALSARTAN

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**Anatomical Therapeutic Chemical (ATC) code**

(C09DX04) valsartan and sacubitril

valsartan and sacubitril

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**Medical condition to be studied**

Myoclonus

## Population studied

**Short description of the study population**

The source population will include all patients present in the database from January 1st, 2015 (first EU approval of sacubitril/valsartan) to 31st December 2023 (or the last available date). All patients will be required to have at least 365 days of observation time before the index date and be 18 years of age or above at index date.

## Documents

**Study report**

[DARWIN EU\\_Report\\_P3-C1-015\\_Sacubitril valsartan and risk of myoclonus V3.pdf](#) (2.33 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)

The Information System for Research in Primary Care (SIDIAP)

IQVIA Disease Analyzer Germany

Clinical Practice Research Datalink (CPRD) GOLD

## Use of a Common Data Model (CDM)

### CDM mapping

Yes

### CDM Mappings

### CDM name

OMOP

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### CDM website

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

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### CDM version

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

## 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**

Unknown