

# DARWIN EU® Drug utilisation of valproate-containing medicinal products in women of childbearing potential

**First published:** 31/01/2023

**Last updated:** 25/09/2024

Study

Finalised

## Administrative details

### EU PAS number

EUPAS50789

### Study ID

84554

### DARWIN EU® study

Yes

### Study countries

☐ Belgium

☐ Finland

☐ Germany

☐ Netherlands

- ☐ Spain
  - ☐ United Kingdom
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### Study description

Valproic acid/valproate-containing medicines are first-line treatment for epilepsy, and used as second-line treatments for the treatment of bipolar disorder and migraine prevention. Valproic acid/valproate is a teratogen, with prenatal exposure carrying a substantial risk of neurodevelopmental impairment and congenital malformations in the child. Therefore, its use in women of childbearing age is restricted to prevent valproate exposure during conception and pregnancy.

The European Medicines Agency commissioned this DARWIN EU© study to estimate the incidence rate and prevalence of VPA use and alternative treatments, and to characterise patient-level valproate use in women between aged  $\geq 12$  to  $\leq 55$  12 and 55 years of age from 2010 to 2022.

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### Study status

Finalised

## 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

## IQVIA NL, Real-World-Evidence

☐ Netherlands

**First published:** 25/11/2022

**Last updated:** 21/03/2025

**Institution**

Other

ENCePP partner

## Fundació Institut Universitari per a la Recerca a l'Atenció Primària de Salut Jordi Gol i Gurina, IDIAPJGol

☐ Spain

**First published:** 05/10/2012

**Last updated:** 23/05/2025

**Institution**

Educational Institution

Laboratory/Research/Testing facility

Not-for-profit

ENCePP partner

## Hospital District of Southwest Finland (HSDF)

☐ Finland

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

**Last updated:** 01/02/2024

**Institution**

**Hospital/Clinic/Other health care facility**

Oxford University UK

## 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

Annika Jodicke [annika.jodicke@ndorms.ox.ac.uk](mailto:annika.jodicke@ndorms.ox.ac.uk)

Study contact

[annika.jodicke@ndorms.ox.ac.uk](mailto:annika.jodicke@ndorms.ox.ac.uk)

### Primary lead investigator

Annika Jodicke

Primary lead investigator

## Study timelines

### Date when funding contract was signed

Planned: 26/07/2022

Actual: 26/07/2022

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### Study start date

Planned: 01/01/2012

Actual: 01/01/2012

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### Date of final study report

Planned: 17/01/2023

Actual: 17/01/2023

## Sources of funding

- EMA

## Study protocol

[D2.2.3\\_DARWIN\\_EU\\_Study\\_Protocol\\_C1-002\\_v2.0\\_Clean\\_EUPAS.pdf](#) (965.28 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:**

Drug utilisation

**Data collection methods:**

Secondary use of data

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**Main study objective:**

1.To characterise the prevalence and incidence of use of valproate, valproate containing medicines, and alternative antiepileptic therapies among women aged 12-55 years of age, stratified by calendar year and age; 2.To characterise the use of valproic acid or valproate containing medicines

## Study Design

**Non-interventional study design**

Cohort

## Study drug and medical condition

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

SODIUM VALPROATE

VALPROATE MAGNESIUM

VALPROATE SEMISODIUM

VALPROIC ACID

VALPROMIDE

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### **Anatomical Therapeutic Chemical (ATC) code**

(N03AG01) valproic acid

valproic acid

(N03AG02) valpromide

valpromide

## Population studied

### **Short description of the study population**

The study included women aged 12-55 years old using valproic acid/valproate-containing medicines between January 2010 and December 2021, with at least 365 days of prior history. The study also included new users with at least 365 days of visibility prior to their first VPA prescription and no previous VPA use.

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### **Age groups**

- Adolescents (12 to < 18 years)
  - Adults (18 to < 46 years)
  - Adults (46 to < 65 years)
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### **Special population of interest**

Pregnant women

Women of childbearing potential using contraception

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### **Estimated number of subjects**

20000

## Study design details



## Outcomes

- 1) Prevalence and incidence of valproate-containing medication and alternative treatments.
  - 2) Patient-level drug utilisation
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## Data analysis plan

The study will be carried out as a Federated Network Analysis Project. All analyses will be conducted separately for each database. The data partners locally execute the analytics and review and approve the by default aggregated results before returning them to the DARWIN EU Coordination Centre. For all analyses a minimum cell count of 5 will be used when reporting results, with any smaller counts obscured. Population level cohort study: Annual prevalence of valproate use and alternative treatments will be estimated, as will annual incidence rates per 100,000 person years. New user cohort study: Large-scale patient-level characterisation will be conducted. Index date will be the date of the first VPA prescription for each person.

## Documents

### Study results

[DARWIN\\_EU\\_Study\\_Report\\_C1-002\\_V2.1.pdf](#) (4.54 MB)

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## 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)

Clinical Practice Research Datalink

Integrated Primary Care Information (IPCI)

The Information System for Research in Primary Care (SIDIAP)

Auria Clinical Informatics (FinOMOP)

IQVIA Longitudinal Patient Data - Belgium

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### Data sources (types)

[Electronic healthcare records \(EHR\)](#)

## 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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## 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