DARWIN EU® Drug utilisation of valproatecontaining medicinal products in women of childbearing potential

First published: 31/01/2023

Last updated: 25/09/2024





Administrative details

EU PAS number	
EUPAS50789	
Study ID	
84554	
DARWIN EU® study	
Yes	
Study countries	
☐ Belgium☐ Finland	
Germany	
Netherlands	

Spain
United Kingdom

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 ≥ 12 to ≤ 55 12 and 55 years of age from 2010 to 2022.

Study status

Finalised

Research institutions and networks

Institutions

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

Netherlands

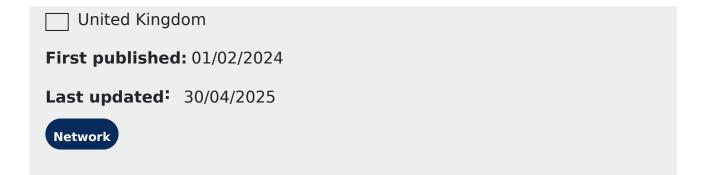
First published: 03/11/2022

Last updated: 02/05/2024
Institution
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
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



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: 26/07/2022 Actual: 26/07/2022

Study start date

Planned: 01/01/2012 Actual: 01/01/2012

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

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

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

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 vaproic 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.

Age groups

- Adolescents (12 to < 18 years)
- Adults (18 to < 46 years)
- Adults (46 to < 65 years)

Special population of interest

Pregnant women

Women of childbearing potential using contraception

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

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)

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

Data sources (types)

Electronic healthcare records (EHR)

Use of a Common Data Model (CDM)

CDM mapping

Yes

CDM Mappings

CDM name

OMOP

CDM website

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

Data quality specifications

Unknown Check completeness Unknown

Check stability

Check conformance

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

No