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

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 | 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

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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

VALPROIC ACID

VALPROMIDE

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

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

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

No