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

First published: 31/01/2023
Last updated: 12/06/2024

Study | Finalised

Administrative details

PURI
https://redirect.ema.europa.eu/resource/84554

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 institution 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

Real-World-Evidence, IQVIA NL

Netherlands
First published: 25/11/2022
Last updated
20/06/2024

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
23/02/2024

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
Hungary
Netherlands
Norway
Portugal
Spain
United Kingdom
First published: 01/02/2024
Last updated
11/06/2024

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 data collection

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
(N03AG02) 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
IPCI
The Information System for Research in Primary Care (SIDIAP)
Auria Clinical Informatics
Longitudinal Patient Data - Belgium

Data sources (types)
Electronic healthcare records (EHR)

Use of a Common Data Model (CDM)

CDM mapping
Yes

Data quality specifications

Check conformance
Unknown

Check completeness
Unknown

Check stability
Unknown

Check logical consistency
Unknown

Data characterisation

Data characterisation conducted
No