Impact of EU label changes and revised pregnancy prevention programme for medicinal products containing valproate: utilisation and prescribing trends

First published: 07/01/2020

Last updated: 01/07/2024

Study Finalised

Administrative details

PURI

https://redirect.ema.europa.eu/resource/49706

EU PAS number

EUPAS31001

Study ID

49706

DARWIN EU® study

No

Study countries

Denmark

Italy

Netherlands

Spain

United Kingdom

Study description

This study will address the research question, “What was the effect of the EU label changes and the revised pregnancy prevention programme (2018) on utilization of valproate containing medicinal products and to what extent did prescribers and patients comply with recommendations?”.

Study status

Finalised

Research institution and networks

Institutions

Division of Pharmacoepidemiology & Clinical Pharmacology (PECP), Utrecht Institute for Pharmaceutical Sciences (UIPS), Utrecht University

Netherlands

First published: 01/03/2010

Last updated: 23/05/2024

Institution **Educational Institution** **ENCePP partner**

Electronic Health Records (EHR) Research Group, London School of Hygiene & Tropical Medicine (LSHTM)

United Kingdom

First published: 19/04/2010

Last updated: 30/10/2024

Institution | Educational Institution | ENCePP partner

Division of Pharmacoepidemiology & Clinical Pharmacology (PECP), Utrecht Institute for Pharmaceutical Sciences (UIPS), Utrecht University

Netherlands

First published: 01/03/2010

Last updated: 23/05/2024

Institution | Educational Institution | ENCePP partner

The PHARMO Institute for Drug Outcomes Research (PHARMO Institute)

Netherlands

First published: 07/01/2022

Last updated: 24/07/2024

Institution | Laboratory/Research/Testing facility | ENCePP partner

Agencia Española de Medicamentos y Productos Sanitarios (Spanish Agency for Medicines and Medical Devices, AEMPS)

Spain

First published: 01/02/2024

Last updated: 04/09/2024

Institution | EU Institution/Body/Agency | Not-for-profit | Regulatory Authority | ENCePP partner

University of Copenhagen Denmark

Networks

EU Pharmacoepidemiology and Pharmacovigilance (PE&PV) Research Network

Netherlands

First published: 01/02/2024

Last updated: 26/11/2024

Network

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Olaf Klungel

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 25/02/2019

Actual: 25/02/2019

Study start date

Planned: 01/10/2020

Actual: 01/10/2020

Data analysis start date

Planned: 01/11/2020

Date of final study report

Planned: 25/02/2022

Actual: 15/08/2022

Sources of funding

- EMA

Study protocol

Protocol Valproates V0.5 SEP2019_uploadversion.pdf(971.82 KB)

AMEND Protocol Valproates V1.1 03DEC2021.pdf(1.27 MB)

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:

Assessment of risk minimisation measure implementation or effectiveness

Drug utilisation

Data collection methods:

Secondary use of data

Main study objective:

This study will address the research question, “What was the effect of the EU label changes and the revised pregnancy prevention programme (2018) on utilization of valproate containing medicinal products and to what extent did prescribers and patients comply with recommendations?”.

Study Design

Non-interventional study design

Cross-sectional

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(N03AG01) valproic acid

(N03AG02) valpromide

Population studied

Short description of the study population

Female subjects of childbearing potential aged 12-55 years using valproate-containing medicinal products identified from the data sources of Netherlands,

UK, Denmark, Italy and Spain between 01 January 2010 and 21 December 2020.

Age groups

Adolescents (12 to < 18 years)

Adults (18 to < 46 years)

Adults (46 to < 65 years)

Special population of interest

Pregnant women

Estimated number of subjects

8000000

Study design details

Outcomes

- valproate use (dispensing/prescription) (objective 1) - pregnancy test (objective 2) - contraceptive use (objective 2) - pregnancy (objective 3) - use of alternative medicines (objective 4), - reason for discontinuation of valproate (objective 1)

Data analysis plan

1. Descriptive and hypothesis testing (objectives 1 and 4) - Incidence rates and quarter-year prevalences of outcomes will be calculated. - Interrupted time series analysis will be performed to test changes in outcomes before vs. after implementation of PRAC intervention. 2. Overall evaluation (objective 5) - The results of objectives 1-4 will be summarized qualitatively.

Documents

Study results

EUPAS31001 Summary.pdf(125.72 KB)

Lot4_Valproates_FinalReport_v3.1_SUMMARY.pdf(176.83 KB)

Study publications

Abtahi S, Pajouheshnia R, Durán CE, Riera-Arnau J, Gamba M, Alsina E, Hoxhaj V,...

Klungel O, Sturkenboom M, Abtahi S, Pajouheshnia R, Durán Salinas C, Riera Arna...

Data management

ENCePP Seal

This study has been awarded the ENCePP seal

Conflicts of interest of investigators

DoIForm_v1.6 valproate klungel.pdf(903.47 KB)

Composition of steering group and observers

Information DoI and steering group EUPAS31001.pdf(92 KB)

Signed code of conduct

2019-0058_Annex 3_Compliance declaration_completed + handtekening.pdf (68.74 KB)

Signed code of conduct checklist

2019-0058_Annex 2_CoC Checklist_completed + handtekening.pdf(397.46 KB)

Signed checklist for study protocols

2019-0058_ENCePPChecklist_Valproates_22AUG2019 FINAL.pdf(165.57 KB)

Data sources

Data source(s)

Clinical Practice Research Datalink

Danish registries (access/analysis)

PHARMO Data Network

BIFAP - Base de Datos para la Investigación Farmacoepidemiológica en el Ámbito Público (Pharmacoepidemiological Research Database for Public Health Systems)

ARS Toscana

Data sources (types)

Administrative data (e.g. claims)

Disease registry

Drug dispensing/prescription data

Electronic healthcare records (EHR)

Use of a Common Data Model (CDM)

CDM mapping

Yes

CDM Mappings

CDM name

ConcepTION CDM

CDM website

https://www.imi-conception.eu/

CDM release frequency

6 months

Data quality specifications

Check conformance

Yes

Check completeness

Yes

Check stability

Yes

Check logical consistency

Yes

Data characterisation

Data characterisation conducted

Yes

Data characterisation moment

after extract-transform-load to a common data model

after creation of study variables"