

Use of antiepileptics and risk of suicidality.  
An exploratory study using the UK General Practice Research Database (GPRD) and data from the Danish registries with an evaluation of available data from further European data sources.

**First published:** 26/10/2012

**Last updated:** 02/07/2024

Study

Finalised

## Administrative details

### EU PAS number

EUPAS2356

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### Study ID

13022

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### DARWIN EU® study

No

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### **Study countries**

- ☐ Denmark
  - ☐ Germany
  - ☐ Netherlands
  - ☐ Spain
  - ☐ United Kingdom
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### **Study description**

The studies described in this protocol are all performed within the framework of PROTECT (Pharmacoepidemiological Research on Outcomes of Therapeutics by a European ConsorTium) Work Package 2 and Working Group 1. The primary aim of these studies is to develop, test and disseminate methodological standards for the design, conduct and analysis of Pharmacoepidemiological (PE) studies applicable to different safety issues and using different data sources. To achieve this, results from PE studies on 5 key Drug / adverse events (D-AEs) pairs performed in different databases will be evaluated. The use of antiepileptics associated with the risk of suicidality is one of the key D-Ae pair of interest. Therefore, emphasis will be on the methodological aspects of the studies in this protocol and not on the clinical consequences of studying the association under investigation.

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### **Study status**

Finalised

## **Research institutions and networks**

### **Institutions**

## F. Hoffmann-La Roche

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

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

Institution

## 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

## European Medicines Agency (EMA)

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

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

Institution

## 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

## Ludwig-Maximilians-University Munich

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

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

**Institution**

Agencia Espanola del Medicamento y Productos Sanitarios (AEMPS) Spain, European Medicines Agency (EMA) United Kingdom, Lægemiddelstyrelsen (Danish Medicines Agency (DKMA) Denmark, Ludwig-Maximilians-Universität-München (LMU MUNCHEN) Germany, F.Hoffmann-La Roche AG Switzerland

## Networks

## PROTECT

- ☐ Belgium
- ☐ Denmark
- ☐ France
- ☐ Germany
- ☐ Italy
- ☐ Netherlands
- ☐ Poland
- ☐ Spain
- ☐ Sweden
- ☐ Switzerland
- ☐ United Kingdom

**First published:** 26/06/2013

**Last updated:** 14/01/2025

Network

## Contact details

### Study institution contact

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Study contact

[markus.schuerch@roche.com](mailto:markus.schuerch@roche.com)

### Primary lead investigator

Markus Schuerch

## Study timelines

### **Date when funding contract was signed**

Planned: 19/08/2009

Actual: 19/08/2009

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### **Study start date**

Planned: 03/10/2011

Actual: 03/10/2011

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### **Date of final study report**

Planned: 31/12/2013

Actual: 01/04/2016

## Sources of funding

- EU institutional research programme
- Pharmaceutical company and other private sector

## More details on funding

Amgen, AstraZeneca, Genzyme, GSK, MerckSerono, Novartis, Roche, Pfizer, Innovative Medicines Initiative (IMI)

## Study protocol

[PROTECT\\_WP2 Final Protocol\\_Suicide\\_Anticonvulsants\\_Dec 16 2011\\_Amend 1 approved 5Oct2012.pdf](#)(457.19 KB)

[PROTECT WP2 Final protocol\\_AED Suicidality\\_Amend3\\_15Feb2013approved.pdf](#)  
(449.55 KB)

## Regulatory

**Was the study required by a regulatory body?**

No

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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:**

Disease /health condition

Human medicinal product

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**Study type:**

Non-interventional study

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**Scope of the study:**

Assessment of risk minimisation measure implementation or effectiveness

Disease epidemiology

Drug utilisation

Other

**If 'other', further details on the scope of the study**

Analysis of discrepancies in results between different databases

**Data collection methods:**

Secondary use of data

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**Main study objective:**

To assess the association between the use of antiepileptics and the risk of suicidality with different study designs across different primary care databases and to compare the results between databases, across designs to evaluate the impact of design/database/population differences on the outcome of the studied association.

## Study Design

**Non-interventional study design**

Cohort

## Study drug and medical condition

**Anatomical Therapeutic Chemical (ATC) code**

(N03A) ANTIEPILEPTICS

ANTIEPILEPTICS

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## Medical condition to be studied

Suicidal behaviour

Suicidal ideation

Completed suicide

Suicide attempt

## Population studied

### Short description of the study population

Patients who have received a first prescription to at least one Antiepileptic drugs (AED) at 1-Jul-1996 or later in the UK or Denmark, age of 15 years and older at the index date, a registration history of at least 6 months prior to the index date (first date of AED prescription) and fulfilling research data criteria in General Practice Research Database (GPRD).

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### Age groups

Infants and toddlers (28 days – 23 months)

Children (2 to < 12 years)

Adolescents (12 to < 18 years)

Adults (18 to < 46 years)

Adults (46 to < 65 years)

Adults (65 to < 75 years)

Adults (75 to < 85 years)

Adults (85 years and over)

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### Estimated number of subjects

55700000

## Study design details

## Data analysis plan

Descriptive studies to compare the six European databases. We will estimate point and period prevalence overall and by AEDs for the study period between 1-Jan-2000 and 31-Dec-2009. Analytical studies to evaluate a possible association between anti-epileptic drugs and suicidality We will estimate risks of suicidality for all AEDs and by individual AEDs prescribed in UK and Denmark. We will apply two different study design: cohort study, and case-crossover studies. For the cohort study we will apply Cox regression analyses with the following potential confounding factors: gender, age, marital status, socio-economic status, BMI, smoking status, alcohol abuse, drug and medication abuse, number of different drugs prescribed in the six months prior to index date, a number of comorbidities associated with a higher risk for suicidality and calendar period. Exposure to AEDs and anti-depressives will be handled as time varying variables.

## Documents

### Study results

[Abstract Schuerch et al \(2016\).pdf](#)(9.75 KB)

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### Study publications

[Schuerch M, Gasse C, Robinson NJ, Alvarez Y, Walls R, Mors O, Christensen J, He...](#)

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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.

### **Signed checklist for study protocols**

[Encepp checklist AED suicidality 31Aug2012 MS.pdf](#)(359.49 KB)

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## Data sources

### **Data source(s)**

THIN® (The Health Improvement Network®)

Clinical Practice Research Datalink

Danish registries (access/analysis)

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### **Data sources (types)**

[Administrative healthcare records \(e.g., claims\)](#)

[Drug dispensing/prescription data](#)

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

## Use of a Common Data Model (CDM)

### **CDM mapping**

No

## 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