# Methods for controlling by indication for prescriptions: application to medications for neuropathic pain

**First published:** 04/10/2021

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

Study Ongoing

## Administrative details

**EU PAS number**

EUPAS43385

**Study ID**

43386

**DARWIN EU® study**

No

**Study countries**

- ☐ Finland
- ☐ France
- ☐ Germany
- ☐ Italy

☐ Norway

☐ United Kingdom

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**Study description**

A large number of different medication groups are used in the treatment of neuropathic pain including gabapentinoids. Besides neuropathic pain, these medications cover a wide range of indications from epilepsy, anxiety, depression, bipolar disorder, etc. As these conditions might carry different risks for the pregnancy, independent of the medications prescribed, it is important to be able to distinguish the reason for their prescribing. Moreover, there are limited data on the safety of use of pregabalin and gabapentin during pregnancy. The project will be divided into three parts: 1. The methodological study aims to develop a general conceptual framework to disentangle the different indications of medications in large healthcare data sources. The methodology will be developed on medications used to treat neuropathic pain. 2. Drug utilisation study aims to characterize the prescription pattern of medications used to treat neuropathic pain among women of childbearing age and pregnant women, focusing on those with limited information regarding the safety profile during pregnancy such as pregabalin and gabapentin. The cohort study will be based on at least 11 data sources, covering 6 at least European countries:France, Finland, Norway, Italy, UK, Germany (approx. 17.7 million pregnancies.) A case-malformed control study will be also performed using the Euromedicat Central database (around 10,5 million pregnancies) 3. Drug safety study aims to assess the association between prenatal exposure to neuropathic pain medications (especially pregabalin and gabapentin) and adverse pregnancy outcomes, including major congenital anomalies, stillbirth, preterm birth, low birth weight, small for gestational age, and long-term neurodevelopmental outcomes. Women aged between 15 and 49 y, from 1 January 2006 to the most recent date of each data source where medications and outcomes data are available wll be studied.

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**Study status**

Ongoing

# Research institutions and networks

## Institutions

### CHU de Toulouse - Hôpital des Enfants

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

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

Institution

### Pharmacoepidemiology and Drug Safety Research Group (PharmaSafe), University of Oslo

Norway

**First published:** 19/10/2016

**Last updated:** 08/11/2016

Institution | Educational Institution | ENCePP partner

### Clinical Practice Research Datalink (CPRD)

United Kingdom

**First published:** 15/03/2010

**Last updated:** 17/01/2025

Institution | Laboratory/Research/Testing facility | ENCePP partner

## Drugs and Pregnancy, Finnish Institute for Health and Welfare (THL)

Finland

**First published:** 17/03/2010

**Last updated:** 20/03/2024

Institution | Educational Institution | Laboratory/Research/Testing facility | ENCePP partner

## Ulster University

United Kingdom (Northern Ireland)

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

**Last updated:** 20/03/2024

Institution | Educational Institution

## University of Bordeaux

France

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

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

Institution | Educational Institution

University of Swansea Wales, UK, University of Ferrara Emilia Romagna, Italy, EUROCAT Ulster University, UK, Institute for prevention Research and epidemiology Leipniz, Germany, University of Bordeaux Bordeaux, France

## Networks

### ConcepTION

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

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Network

## Contact details

**Study institution contact**

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**Primary lead investigator**

Christine Damase-Michel

**Primary lead investigator**

## Study timelines

**Date when funding contract was signed**

Planned: 01/04/2019

Actual: 01/04/2019

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**Study start date**

Actual: 08/05/2021

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**Date of final study report**

Planned: 31/03/2024

## Sources of funding

- EU institutional research programme

## More details on funding

IMI ConcePTION

## 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 type:**

Non-interventional study

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**Scope of the study:**

Assessment of risk minimisation measure implementation or effectiveness

Drug utilisation

**Main study objective:**

1. to develop a general conceptual framework to disentangle the different indications of medications in large healthcare data sources. 2.to characterize the prescription pattern of medications used to treat neuropathic pain among women of childbearing age and pregnant women 3.to assess the association between prenatal exposure to neuropathic pain medications and adverse pregnancy outcomes.

## Study Design

**Non-interventional study design**

Case-control

Cohort

## Study drug and medical condition

**Anatomical Therapeutic Chemical (ATC) code**

(N03AX12) gabapentin

gabapentin

(N03AX16) pregabalin

pregabalin

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**Medical condition to be studied**

Neuralgia

## Population studied

**Age groups**

Adolescents (12 to < 18 years)

Adults (18 to < 46 years)

Adults (46 to < 65 years)

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**Special population of interest**

Pregnant women

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**Estimated number of subjects**

6800000

## Study design details

**Outcomes**

major congenital anomalies, stillbirth, preterm birth, low birth weight, small for gestational age, long-term neurodevelopmental outcomes

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**Data analysis plan**

Drug utilisation study: prevalence of medications of interest prescribed among women of childbearing age and among pregnant women, stratified by age, calendar year, data sources, and indication for prescribing Drug safety study: - cohort study : comparing “exposed” and “comparison” women. The analyses will be carried out using multivariate logistic regression, and survival analysis, depending on the outcome of interest to calculate unadjusted and adjusted odds ratios (ORs) and hazard ratios (HRs), along with 95% confidence intervals (CI). Advanced confounder adjustment methods (such as propensity score methods) might be used when appropriate to further mitigate measured confounding. - case-malformed control study using data from EUROmediCAT. We will conduct an exploratory analysis in which, for each analysis, we will consider a single EUROCAT subgroup of congenital anomaly to be the “case” group, excluding those with chromosomal conditions. Logistic regression will be used.

# 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

EFEMERIS

German Pharmacoepidemiological Research Database

ARS Toscana

EUROmediCAT central database

SAIL Databank

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**Data source(s), other**

CPRD, NorPD, Emilia Romagna GPs drug prescription, EFEMERIS, Drugs and Pregnancy Finland, GePaRD, ARS, EUROmediCAT, SAIL databank

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**Data sources (types)**

Administrative healthcare records (e.g., claims)

Drug dispensing/prescription data

Other

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**Data sources (types), other**

Exposure registry

## Use of a Common Data Model (CDM)

**CDM mapping**

No

## Data quality specifications

**Check conformance**

Unknown

**Check completeness**

Unknown

**Check stability**

Unknown

**Check logical consistency**

Unknown

## Data characterisation

**Data characterisation conducted**

No