DARWIN EU® – Utilisation of commonly used benzodiazepines during pregnancy and the incidence of pregnancy losses

First published: 02/04/2025

Last updated: 10/04/2025

Study Ongoing

Administrative details

PURI

https://redirect.ema.europa.eu/resource/1000000536

EU PAS number

EUPAS1000000536

Study ID

1000000536

DARWIN EU® study

Yes

Study countries

☐ Norway

Spain

Study description

Benzodiazepines are commonly prescribed for their anxiolytic, hypnotic, and sedative effects. Despite the use of benzodiazepines during pregnancy, there is limited evidence to support their use during this period or to favor their use over alternative treatments that may provide similar symptom relief with differing safety profiles. Understanding the patterns of benzodiazepine use during pregnancy in Europe, together with the rates of pregnancy losses, is essential for evaluating safety and effectiveness.

Despite detailed pregnancy information in many data sources, pregnancy episodes in electronic health record (EHR) data are often inconsistently coded across sources.

As part of the upcoming benzodiazepines periodic safety update report single assessment (PSUSA), the Pharmacovigilance Risk Assessment Committee (PRAC) has requested real-world evidence (RWE) on the utilisation of commonly used benzodiazepines during pregnancy.

Additionally, the background rates of pregnancy losses will be described to help contextualise the assessment of treatment safety during pregnancy.

To date, two data partners within the DARWIN EU® Data Network have pre-processed pregnancy episodes and developed a Pregnancy Extension Table (PET).

While the table has been successfully employed in other contexts, this study marks the first application of this table within the DARWIN EU® Data Network.

Study status

Ongoing

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

Networks

Data Analysis and Real World Interrogation Network (DARWIN EU®)

- [ ] Belgium
- [ ] Croatia
- [ ] Denmark
- [ ] Estonia
- [ ] Finland
- [ ] France
- [ ] Germany
- [ ] Hungary
- [ ] Netherlands
- [ ] Norway
- [ ] Portugal
- [ ] Spain

United Kingdom

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Network

Contact details

Study institution contact

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Primary lead investigator

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Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 16/07/2024

Actual: 16/07/2024

Study start date

Planned: 16/07/2024

Actual: 16/07/2024

Date of final study report

Planned: 30/09/2025

Sources of funding

- EMA

Study protocol

DARWIN EU_Protocol_P3-C3-009_Bromazepam_V2.pdf(1015.03 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

Data collection methods:

Secondary use of data

Study design:

Population-level cohort

Drug/s user cohort

Population-level cohort

Cohort analysis

Main study objective:

1. To characterise users of benzodiazepine and alternative treatments (SSRIs, SNRIs, Z-hypnotics, and Melatonin) during pregnancy in terms of demographics, prior medications, history of mental illness and other comorbidities.
2. To characterise treatments with benzodiazepine and alternative treatments during pregnancy in terms of duration, posology, and indication of prescription during pregnancy.
3. To describe the prevalence of benzodiazepine and alternative treatments' use during pregnancy
4. To describe trajectories of prescriptions fills for benzodiazepine and alternative treatments throughout the year before pregnancy, pregnancy period, and one month following pregnancy end date.
5. To estimate the incidence of pregnancy loss among all pregnancies and in benzodiazepines and alternative treatment users during pregnancy (when numbers allow).
6. To characterise individuals with pregnancy loss in terms of demographics, comorbidities, and treatments of interest.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Name of medicine, other

Commonly used benzodiazepines

Population studied

Short description of the study population

Participants in the study will be required to fulfil the following criteria:

Inclusion criteria (Table 5):

1) Observation period within the study period (1st January 2010-31st December 2023, or latest data availability).

2) Female sex at birth.

3) At least one year of prior history recorded before start of pregnancy episode.

4) A pregnancy episode recorded during the study period (defined by the pregnancy start date), with a pregnancy start date on or before December 31, 2022 (to allow sufficient time between index date and last date of database data availability to cover a full-term pregnancy).(29)

5) Pregnancy end date follows pregnancy start date (in time).

6) Pregnancy duration (in days) is greater than 1 but less than 308 days (equivalent to 44 weeks of gestation).

Exclusion criteria (Table 6):

1) Molar and ectopic pregnancies will be excluded (concept ids: 439083 and 437611).

Disease Epidemiology (objective 5): Two approaches will be used:

• No exclusion for prior history of pregnancy

• Excluding anyone with a history of pregnancy in the -365 days.
• Excluding anyone with an unknown pregnancy outcome.

Data management

Data sources

Data source(s)

Norwegian Linked Health registry at University of Oslo

The Information System for Research in Primary Care (SIDIAP)

Use of a Common Data Model (CDM)

CDM mapping

Yes

CDM Mappings

CDM name

OMOP

CDM website

https://www.ohdsi.org/Data-standardization/

CDM version

https://ohdsi.github.io/CommonDataModel/index.html

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

Unknown