Long-term cardiovascular safety and real-world use of eptinezumab - An observational, historical cohort study of patients initiating eptinezumab in routine clinical practice

First published: 28/01/2026

Last updated: 28/01/2026

Study Planned

Administrative details

EU PAS number

EUPAS1000000882

Study ID

1000000882

DARWIN EU® study

No

Study countries

- ☐ Denmark
- ☐ Germany

- [ ] Italy
- [ ] United States

Study description

This post-authorisation safety study (PASS) will be conducted using longitudinal healthcare databases. It uses a historical comparative cohort study design and will include migraine patients treated with eptinezumab in routine clinical practice and followed-up for a maximum of six years from exposure start. In addition, control cohorts of migraine patients without exposure to eptinezumab will be identified. Major adverse cardiovascular events (MACE), defined as nonfatal stroke, nonfatal acute coronary syndrome, or cardiovascular death, will be the primary study outcome. The risk of MACE in patients treated with eptinezumab will be compared with the risk in control cohorts of patients with migraine who were not treated with eptinezumab. All analyses will be performed separately in each included healthcare databases. The risk estimates from the individual healthcare databases will then be pooled in meta-analyses to increase statistical power of the final combined analysis.

Study status

Planned

Research institutions and networks

Institutions

RTI Health Solutions (RTI-HS)

- [ ] France
- [ ] Spain
- [ ] Sweden

- [ ] United Kingdom
- [ ] United Kingdom (Northern Ireland)
- [ ] United States

First published: 21/04/2010

Last updated: 13/03/2025

Institution | Not-for-profit | ENCePP partner

H. Lundbeck

First published: 01/02/2024

Last updated: 01/02/2024

Institution

Contact details

Study institution contact

Non-interventional Research Manager H. Lundbeck A/S - Observational Research Committee

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Study contact

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Primary lead investigator

H. Lundbeck A/S Non-interventional Research Manager

Primary lead investigator

Study timelines

Date when funding contract was signed
Planned: 30/11/2025

Study start date
Planned: 01/05/2026

Data analysis start date
Planned: 01/05/2026

Date of interim report, if expected
Planned: 30/06/2026

Date of final study report
Planned: 31/12/2030

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

H. Lundbeck A/S

Regulatory

Was the study required by a regulatory body?

Yes

Is the study required by a Risk Management Plan (RMP)?

EU RMP category 3 (required)

Methodological aspects

Study type

Study type list

Study topic:

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Safety study (incl. comparative)

Data collection methods:

Secondary use of data

Main study objective:

To assess the long-term cardiovascular risk in migraine patients treated with eptinezumab, in comparison to appropriate control cohorts of patients with migraine who were not treated with eptinezumab. To evaluate the long-term cardiovascular risk in migraine patients with a known history of cardiovascular disease using eptinezumab in comparison to migraine patients with a known history of cardiovascular disease not using eptinezumab.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Medicinal product name

VYEPTI

Study drug International non-proprietary name (INN) or common name

EPTINEZUMAB

Anatomical Therapeutic Chemical (ATC) code

(N02CD05) eptinezumab

eptinezumab

Medical condition to be studied

Migraine

Population studied

Short description of the study population

Patients with migraine, treated with eptinezumab or other preventive migraine medications

Special population of interest

Other

Special population of interest, other

Migraine

Estimated number of subjects

28394

Study design details

Setting

The study will include migraine patients treated with eptinezumab in routine clinical practice and followed-up for a maximum of six years from exposure start. The following control cohorts will be identified: 1. A cohort of migraine patients treated with non-CGRP targeting preventive migraine medications; 2. a cohort of migraine patients not treated with any preventive migraine medication; and 3. a cohort of migraine patients representing standard-of-care. The study inclusion period will be from eptinezumab launch date in the respective country until 31 December 2026.

Comparators

1. non-GCRP preventive migraine medications; 2. no exposure to preventive migraine medications; 3. migraine standard-of-care

Outcomes

Primary outcome: major adverse cardiovascular events (MACE), defined as nonfatal stroke, nonfatal acute coronary syndrome, or cardiovascular death. Secondary outcomes: non-fatal stroke; stroke; ischemic stroke; non-fatal ACS; ACS; CV death; transitory ischemic attack (TIA); angina pectoris (all subtypes, i.e. independently from coding of stable/instable); percutaneous coronary intervention (PCI); heart failure.

Data analysis plan

After identification of the study cohorts, cohort balancing (i.e. identification of appropriate control cohorts) will be performed within a propensity score-based approach. Study analyses will be done in the sequence of ‘cohort balancing’ followed by the ‘cohort analyses’ in the unbalanced and balanced cohorts. Hazard ratios of the primary and secondary study outcomes, along with their 95% confidence intervals, will be estimated to assess the long-term cardiovascular risk in patients treated with eptinezumab, in comparison to each control cohort. For each of the three comparisons (EE vs. MEC; EE vs. MNEC; EE vs. SoC), hazard ratios will be estimated for the unbalanced and the balanced study cohorts using COX proportional hazard regression analysis. In addition, cumulative incidences will be estimated for the unbalanced and balanced cohorts. Subgroup analyses will be performed to evaluate the impact of a known history of cardiovascular diseases on the long-term cardiovascular risk in patients using eptinezumab in clinical practice, as well as the impact of migraine disease severity.

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)

German Pharmacoepidemiological Research Database

Danish Health Data Registries

Data source(s), other

US healthcare database

Data sources (types)

Administrative healthcare records (e.g., claims)

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