Lamotrigine use in Pregnancy and Risk of Orofacial Clefts

First published: 16/02/2015

Last updated: 16/02/2015

Study Finalised

Administrative details

EU PAS number

EUPAS8615

Study ID

8616

DARWIN EU® study

No

Study countries

- Belgium
- Croatia
- Denmark
- France
- Germany
- Ireland

Italy
Malta
Netherlands
Norway
Poland
Spain
Switzerland
United Kingdom

Study description

A case-malformed control study evaluating the risk of orofacial clefts in relation to first trimester exposure to the the new anti-epileptic drug (AED) lamotrigine was conducted using data from 19 EUROCAT registries covering a population of 4 million births, 1995-2005. The study found no evidence of a specific increased risk of isolated orofacial clefts relative to other malformations due to lamotrigine monotherapy. This study was conducted following a US Federal Drugs Agency alert in 2006 concerning an increased risk of orofacial cleft associated with lamotrigine exposure.

Study status

Finalised

Research institutions and networks

Institutions

Ulster University

United Kingdom (Northern Ireland)

First published: 01/02/2024

Last updated: 20/03/2024

Institution | Educational Institution

Networks

European Surveillance of Congenital Anomalies (EUROCAT)

- Austria
- Belgium
- Croatia
- Czechia
- Denmark
- Finland
- France
- Germany
- Hungary
- Ireland
- Italy
- Malta
- Netherlands
- Norway
- Poland
- Portugal
- Spain
- Sweden

Switzerland

United Kingdom

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Network | ENCePP partner

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Helen Dolk

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 07/02/2007

Actual: 07/02/2007

Study start date

Actual: 15/02/2007

Data analysis start date
Actual: 18/04/2007

Date of final study report
Actual: 31/07/2007

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

GSK

Regulatory

Was the study required by a regulatory body?

No

Methodological aspects

Study type

Study type list

Study topic:

Human medicinal product

Disease /health condition

Study type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Data collection methods:

Secondary use of data

Main study objective:

To investigate in a large dataset whether lamotrigine exposure in the first trimester of pregnancy is associated with an increased risk of orofacial clefts relative to other malformations

Study Design

Non-interventional study design

Case-control

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(N03AX09) lamotrigine

lamotrigine

Medical condition to be studied

Cleft lip and palate

Cleft palate

Population studied

Short description of the study population

Pregnant women who had first trimester exposure to the new anti-epileptic drug (AED) lamotrigine.

Age groups

- Preterm newborn infants (0 – 27 days)
- Term newborn infants (0 – 27 days)
- Infants and toddlers (28 days – 23 months)

Special population of interest

Pregnant women

Estimated number of subjects

85.563

Study design details

Outcomes

Odds of lamotrigine (LMT) exposure among OC registrations (cases) was compared with the odds of LTG exposure among malformed non-OC registrations (controls). An exploratory hypothesis-generating analysis compared the proportion of different malformation subgroups, according to EUROCAT subgroup definitions,among all nonchromosomal registrations, between lamotrigine exposed (all and mono) and AED unexposed registrations.

Data analysis plan

Crude ORs were calculated ignoring the registry of origin. In order to analyze the data taking into account the registry and including all registries (even if they had no exposure to lamotrigine (LMG) in either cases or controls) the WinBUGS computer package was used to fit multinomial responses with a logistic link. Maternal age was treated as a categorical variable. Due to the small numbers of exposures to LTG it was not possible to adjust simultaneously for both registry and maternal age.

Documents

Study publications

Dolk H, Jentink J, Loane M, Morris J, de Jong-van den Berg LTW and EUROCAT Anti...

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)

European network of population-based registries for the epidemiological surveillance of congenital anomalies

Data sources (types)

Disease 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