The risk of ischemic cardiovascular events associated with oxycodone/naloxone use

First published: 29/09/2014

Last updated: 01/04/2024

Study Finalised

Administrative details

EU PAS number

EUPAS7545

Study ID

29020

DARWIN EU® study

No

Study countries

☐ Germany

Study description

Opioid-induced constipation (OIC) is one of the most common adverse effects of opioid therapy and several approaches have been made to reverse OIC without compromising pain relief. Targin® is an oral fixed combination of the extended-

release (ER) high potency opioid (HPO) oxycodone and the opioid antagonist naloxone. It is approved in Germany for the treatment of severe pain and has been proven to provide comparable analgesic efficacy to that of oxycodone, while improving OIC. However, the long-term safety of opioid antagonists is not clear. The FDA for example expressed concerns over potential cardiac safety risks associated with use of opioid antagonists discussing withdrawal as possible cause for these risks. This study will estimate the risk of cardiovascular events such as myocardial infarction or ischemic stroke in patients receiving oxycodone/naloxone compared to those being treated with ER oxycodone or another ER HPO.

Study status

Finalised

Research institutions and networks

Institutions

Leibniz Institute for Prevention Research and Epidemiology - BIPS

Germany

First published: 29/03/2010

Last updated: 26/02/2024

Institution **Not-for-profit** **ENCePP partner**

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Tania Schink

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 08/09/2013

Actual: 08/09/2013

Study start date

Planned: 01/01/2004

Actual: 01/01/2004

Data analysis start date

Planned: 15/04/2014

Actual: 15/04/2014

Date of interim report, if expected

Planned: 15/10/2014

Actual: 05/12/2014

Date of final study report

Planned: 31/12/2014

Actual: 31/12/2014

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Purdue Pharma L.P.

Regulatory

Was the study required by a regulatory body?

No

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

Study type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Drug utilisation

Data collection methods:

Secondary use of data

Main study objective:

The main study objective is to estimate the risk of ischemic Cardiovascular (CV) events in patients receiving Targin® compared to those being prescribed extended-release (ER) oxycodone or another ER high potency opioid (HPO).

Study Design

Non-interventional study design

Case-control

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(N02AA) Natural opium alkaloids

Natural opium alkaloids

(N02AA01) morphine

morphine

(N02AA03) hydromorphone

hydromorphone

(N02AA05) oxycodone

oxycodone

(N02AB03) fentanyl

fentanyl

(N02AE01) buprenorphine

buprenorphine

(N02AG04) hydromorphone and antispasmodics

hydromorphone and antispasmodics

(N02AX06) tapentadol

tapentadol

Medical condition to be studied

Acute myocardial infarction

Ischaemic stroke

Population studied

Short description of the study population

Patients prescribed with extended-release (ER) high potency opioid (HPO) during January 01, 2006 to December 31, 2011.

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)

Estimated number of subjects

300000

Study design details

Outcomes

The primary outcome is the combined endpoint of acute myocardial Infarction (MI) or acute ischemic stroke (IS). The secondary outcome will be based on a broader outcome definition examining additional ischemic CV events such as angina or transient ischemic attacks.

Data analysis plan

Cohort entry is defined as the first dispensation of an extended-release high potency opioid (ER HPO). Baseline covariates will be assessed in the year preceding cohort entry. In the cohort analyses, first a drug utilization part including characteristics of HPO users as well as patterns of opioid use will be conducted. Furthermore two models will be established examining predictive factors for (i) the choice of ER HPO and (ii) for the occurrence of ischemic cardiovascular events. Following this, incidence rates overall and stratified for baseline covariates will be calculated for the outcomes in users of Targin®, ER oxycodone, ER morphine and other extended-release HPO, including patches. Additionally, a nested case-control analysis within this user cohort will be conducted to obtain confounder-adjusted estimates for the risk of myocardial

infarction and ischemic stroke associated with (i) current HPO treatment or (ii) recent discontinuation or (iii) recent switch of HPO therapy.

Documents

Study results

Targin_Report_Abstract.pdf (19.42 KB)

Study publications

Jobski, K., Kollhorst, B., Schink, T. et al. The Risk of Opioid Intoxications o...

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

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

Unknown