

# Post-authorisation Safety Study: Risk of Out-of-Hospital Sudden Cardiac Death in Users of Domperidone, Users of Proton Pump Inhibitors, and Users of Metoclopramide

**First published:** 28/02/2013

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

Study

Finalised

## Administrative details

### PURI

<https://redirect.ema.europa.eu/resource/24330>

### EU PAS number

EUPAS3590

### Study ID

24330

### DARWIN EU® study

No

### Study countries

United Kingdom

### Study description

The overall goal of this research study is to find out whether use of domperidone, a gastrointestinal medication taken for symptoms of nausea and vomiting, may increase the chance of out-of-hospital sudden cardiac death (SCD) compared with the use of two other gastrointestinal medications, the proton pump inhibitor (PPI) medications as a group and metoclopramide, and during periods of non-use of all three types of study medications. Earlier studies have found an increased risk of SCD or a combined outcome of SCD and severe ventricular arrhythmia with current use of domperidone compared with non-use.

Evidence from these studies suggested that risk was increased among persons aged older than 60 years and among those receiving a dose of more than 30 mg of domperidone per day orally, but there were not enough exposed individuals for a definitive answer to these questions. The current study will contribute additional information by providing an in-depth analysis of the risk of SCD in relation to domperidone by age and dose. To improve on previous studies it is designed as a nested case control and will include metoclopramide use as a comparator medication in addition to PPI medications, and a case-cross over analysis in which each subject will serve as his/her own control. The study will be performed in the CPRD linkable to Health Episode Statistics data. An important goal of the study is to examine whether higher doses of domperidone are related to higher risk of SCD than lower doses or whether patients using domperidone for longer periods of time are at higher risk. For some patients, the information needed to calculate daily dose of domperidone or length of domperidone use may be missing in the electronic database. For these patients, the researchers plan to conduct a survey of their general practitioners to gather information about dose and duration of exposure. The results of the study will be presented in a study report and in a peer reviewed manuscript.

## Study status

Finalised

## Research institution 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

19/02/2024

Institution

Not-for-profit

ENCePP partner

## Contact details

### Study institution contact

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Study contact

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**Primary lead investigator**

**Alejandro Arana**

Primary lead investigator

## Study timelines

### **Date when funding contract was signed**

Actual:

24/07/2012

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### **Study start date**

Planned:

01/01/2013

Actual:

25/01/2013

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### **Data analysis start date**

Planned:

28/01/2013

Actual:

20/02/2013

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### **Date of final study report**

Planned:

21/12/2013

Actual:

22/08/2014

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## Sources of funding

- Pharmaceutical company and other private sector

## More details on funding

Janssen Research and Development, L.L.C.

## Study protocol

[0303209 Final Protocol\\_V1.1\\_signed.pdf](#)(717.61 KB)

[0303209 Final Protocol\\_V1.1\\_blackout.pdf](#)(744.28 KB)

## Regulatory

**Was the study required by a regulatory body?**

Yes

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

Not applicable

## Methodological aspects

### Study type

#### Study type list

**Study topic:**

Human medicinal product

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**Study type:**

Non-interventional study

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**Scope of the study:**

Assessment of risk minimisation measure implementation or effectiveness

**Data collection methods:**

Secondary data collection

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**Main study objective:**

The research goal is to assess the risk of out-of-hospital Sudden cardiac death (SCD) associated with current use of domperidone compared with the risk in periods of non-use of domperidone or use of other gastrointestinal medications. Of particular interest is the assessment of risk of SCD in relation to estimated daily dose of domperidone and to age.

## Study Design

## Non-interventional study design

Case-control

Cohort

Other

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## Non-interventional study design, other

Case-crossover

# Study drug and medical condition

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

DOMPERIDONE

# Population studied

## Short description of the study population

Patients from a single database in the UK, the CPRD, for the years 2005 through 2011 who were at the risk of sudden cardiac death.

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## Age groups

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)

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## Estimated number of subjects

15000

# Study design details

## Outcomes

The endpoint of the study is SCD that occurs outside a hospital or other institutional setting.

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## Data analysis plan

The absolute risk of SCD will be estimated as the number of SCD events divided by the person-years of follow-up. Incidence rates of SCD stratified by the following factors (Sex, age group, and diabetes status) will be calculated for current use of domperidone, current use of PPI medications, current use of metoclopramide, and non-use of any of these medications. Incidence rate ratios will be calculated comparing current use of domperidone with current use of PPI medications, current use of metoclopramide, and with non-use time,

standardised for age and sex. For domperidone users, incidence rates will also be stratified by dose categories and dose-response trend explored. Multivariable conditional logistic regression will be used to estimate the risk of SCD from current domperidone exposure adjusted by potential confounders. A case-crossover analysis in the cases of SCD will allow further control of confounding

## Documents

### Study publications

[Arana A, Johannes C, Varas C, Rothman KJ, McQuay L, Yang Q. Assessment of daily...](#)

[Arana A, Johannes CB, McQuay LJ, Varas-Lorenzo C, Fife D. Risk of Out-of-Hospit...](#)

[Varas-Lorenzo C, Arana A, Johannes CB, McQuay LJ, Rothman KJ, Fife D. Improving...](#)

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## Data management

### ENCePP Seal

#### Signed checklist for study protocols

[ENCePP Check list for Study Protocols \(Revision2\)\\_5Mar2013.pdf](#) (1.58 MB)

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## Data sources

### Data source(s)

Clinical Practice Research Datalink

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### Data sources (types)

[Electronic healthcare records \(EHR\)](#)

## Use of a Common Data Model (CDM)

### CDM mapping

No

## Data quality specifications

### Check conformance

Unknown

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**Check completeness**

Unknown

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**Check stability**

Unknown

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**Check logical consistency**

Unknown

**Data characterisation**

**Data characterisation conducted**

Unknown