

# Impact of EU label changes for hydroxyzine products: post-referral prescribing trends

**First published:** 03/12/2018

**Last updated:** 17/05/2024

Study

Finalised

## Administrative details

### EU PAS number

EUPAS26363

### Study ID

38866

### DARWIN EU® study

No

### Study countries

- ☐ Denmark
- ☐ Netherlands
- ☐ United Kingdom

### Study description

To evaluate the impact of the risk minimisation measures implemented in 2015 to manage the potential risk of QT interval prolongation and cardiac arrhythmia of hydroxyzine containing medicinal products authorised in the European Union (EU) in clinical practice.

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## Study status

Finalised

## Research institutions and networks

### Institutions

#### MEMO Research, University of Dundee

☐ United Kingdom (Northern Ireland)

**First published:** 12/05/2010

**Last updated:** 17/05/2024

Institution

Educational Institution

Not-for-profit

ENCePP partner

#### UCL School of Pharmacy, University College London

☐ United Kingdom

**First published:** 11/03/2010

**Last updated:** 21/04/2015

Institution

Outdated

Educational Institution

ENCePP partner

# The PHARMO Institute for Drug Outcomes Research (PHARMO Institute)

☐ Netherlands

**First published:** 07/01/2022

**Last updated:** 19/12/2025

**Institution**

**Non-Pharmaceutical company**

**ENCePP partner**

NHS National Services Scotland Glasgow, UK,  
University of Southern Denmark Denmark,  
University of Strathclyde Glasgow

## Contact details

### Study institution contact

Thomas MacDonald [t.m.macdonald@dundee.ac.uk](mailto:t.m.macdonald@dundee.ac.uk)

**Study contact**

[t.m.macdonald@dundee.ac.uk](mailto:t.m.macdonald@dundee.ac.uk)

### Primary lead investigator

Thomas MacDonald

**Primary lead investigator**

# Study timelines

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

Planned: 22/03/2018

Actual: 22/03/2018

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## **Study start date**

Planned: 01/07/2019

Actual: 01/07/2019

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## **Date of final study report**

Planned: 23/08/2019

Actual: 22/09/2019

# Sources of funding

- EMA

# Study protocol

[Study Protocol Hydroxyzine\\_20072018 clean.pdf](#) (329.4 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 topic:**

Human medicinal product

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**Study type:**

Non-interventional study

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**Scope of the study:**

Drug utilisation

Effectiveness study (incl. comparative)

**Data collection methods:**

Secondary use of data

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**Main study objective:**

The three main objectives are as follows: To determine prescription patterns of hydroxyzine containing products. To determine prescribers compliance with recommendations. To determine prescription patterns of alternative medicines prescribed in patients where hydroxyzine has previously been prescribed.

## Study Design

**Non-interventional study design**

Cohort

Other

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**Non-interventional study design, other**

Population-based longitudinal study, Time series analysis

## Study drug and medical condition

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

## Population studied

### **Short description of the study population**

The study population consisted of all patients registered within each data source at any time during the study period. The start of follow-up for a patient was defined as date of registration with the general practice (CPRD and PHARMO), or date of first recorded prescription or any secondary care diagnosis (Denmark and

Scotland). A patient's index date was the latest of the study period start date (dependent on each data source), the date of birth, or their first database follow up date plus 1 year (to allow sufficient time for data on baseline covariates to be collected). A patient's end of follow-up was the date of the first occurrence of the following: death (all databases); end of study period (varies between countries); end of registration (end of registration would not significantly affect data from Denmark and Scotland because they use national data that captures patients moving within the health system). A patient was included for analysis in a time period if the first and last day both lay between the patient's index date and their last follow up date, so the analyses only included patients who are observable for the entire timeperiod.

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### **Age groups**

- Term newborn infants (0 - 27 days)
- 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)
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### **Estimated number of subjects**

100000

## Study design details

### **Data analysis plan**

The proposed primary analysis will address the three objectives given above using interrupted time series regression to fit time trends to each series of time period data for each country. Using regression modelling we will evaluate: (1) The baseline slope before the intervention time point, (2) The change in slope from the baseline trend to the post-intervention trend, (3) The immediate change associated with the intervention time point. The effect of the intervention for each country will be represented either by a step function, or by a continuous linear function representing gradual implementation (interrupted time series analysis). This choice, and whether it is necessary to model any trends prior to the intervention time point, will be decided on visual inspection of the data. The analysis will be done by data source initially, and only pooled if the statistical models do not differ significantly between data sources.

## Documents

### **Study results**

[EMA\\_hydroxyzine\\_final revised\\_061219.pdf](#) (889.11 KB)

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## Study, other information

[Hydroxyzine abstract\\_Final\\_040320.pdf](#) (91.03 KB)

## Study publications

[Morales DR, Macfarlane T, MacDonald TM, Hallas J, Ernst MT, Herings RM, Smits E...](#)

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## 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.

This study has been awarded the ENCePP seal

## Conflicts of interest of investigators

[DoI\\_UoD\\_TMM\\_011118.pdf](#) (911.35 KB)

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## Composition of steering group and observers

[Steering Group\\_Hydroxyzine\\_May18v1.pdf](#) (10.15 KB)

[Steering Group\\_Hydroxyzine\\_V2\\_Dec18.pdf](#) (10.25 KB)

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## Signed code of conduct

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## Signed code of conduct checklist



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### **Signed checklist for study protocols**

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## Data sources

### **Data source(s)**

Clinical Practice Research Datalink

Danish registries (access/analysis)

PHARMO Data Network

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### **Data source(s), other**

eDRIS

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### **Data sources (types)**

[Drug dispensing/prescription data](#)

[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**

No