Ranitidine and other histamine H2-receptor antagonists – a drug utilisation study

First published: 03/02/2020
Last updated: 02/05/2024

Study | Finalised

Administrative details

PURI
https://redirect.ema.europa.eu/resource/39072

EU PAS number
EUPAS33397

Study ID
39072

DARWIN EU® study
No

Study countries
Belgium
France
Germany
Netherlands
Spain
United Kingdom

Study description
Results of a preliminary laboratory analysis have shown the presence of N-Nitrosodimethylamine (NDMA), a human carcinogen, in ranitidine. At the request of the European Commission, the EMA's Committee for Medicinal Products for Human Use (CHMP) is evaluating all available data to assess whether patients using ranitidine are at any risk from NDMA and whether regulatory action is warranted at EU level to protect

patients and public health. Data about prescribing and use patterns of ranitidine-containing medicines in EU Member States will inform on the population at risk of exposure to NDMA (or other nitrosamines) through use of ranitidine. It will also provide information on usage patterns for different substances of the class informing on usage of substances alternative to ranitidine. By means of a retrospective cohort study we aim to: i) study the prevalence and incidence of exposure to H2-receptor antagonists as a class and by individual ingredient, ii) explore the characteristics of H2-receptor antagonist use in terms of observation time, cumulative duration, cumulative dose and cumulative annual dose for the class as a whole and by individual ingredient with regard to age, sex, formulation, daily dose iii) explore the indication of use of H2-receptor antagonist by class level, individual ingredient and by formulation, iv) explore the proportion of patients treated with H2-receptor antagonists suffering from renal impairment. For this study, we will include Electronic Healthcare Record data from six primary care databases throughout Europe: IPCI (the Netherlands), SIDIAP (Spain), IMRD (UK), LPD (Belgium), DA Germany and DA France. All these databases have their data mapped to the OMOP Common Data Model.

Study status
Finalised

Research institution and networks

Institutions

Department of Medical Informatics - Health Data Science, Erasmus Medical Center (ErasmusMC)

Netherlands
First published: 03/11/2022
Last updated 02/05/2024

Institution | Educational Institution | ENCePP partner

IQVIA

United Kingdom
First published: 12/11/2021
Last updated 22/04/2024

Institution | Non-Pharmaceutical company | ENCePP partner

Fundació Institut Universitari per a la Recerca a l'Atenció Primària de Salut Jordi Gol i Gurina, IDIAPJGol

Spain
First published: 05/10/2012
Last updated
23/02/2024

Institution
Educational Institution
Laboratory/Research/Testing facility
Not-for-profit
ENCePP partner

Contact details

Study institution contact
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Study contact

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Primary lead investigator
Katia Verhamme
Primary lead investigator

Study timelines

Date when funding contract was signed
Planned:
25/11/2019
Actual:
25/11/2019

Study start date
Planned:
20/01/2020
Actual:
20/01/2020

Data analysis start date
Planned:
15/02/2020

Actual:
15/02/2020

Date of interim report, if expected
Planned:
13/03/2020
Actual:
13/03/2019

Date of final study report
Planned:
27/03/2020
Actual:
07/04/2020

Sources of funding

- EMA

Study protocol

ranitidine protocol_17Januari2020_FINAL_clean.pdf(1.56 MB)

Regulatory

Was the study required by a regulatory body?
Yes

Is the study required by a Risk Management Plan (RMP)?
Not applicable

Methodological aspects

Study type

Study type list

Study topic:
Human medicinal product

Study type:
Non-interventional study

Scope of the study:
Drug utilisation

Data collection methods:
Secondary data collection

Main study objective:
1/ To study the prevalence and incidence of exposure to H2-receptor antagonists (H2RA) as a class and by individual ingredient2/ To explore the characteristics of H2RA use 3/ To explore the indication of use of H2RA by class level, individual ingredient and by formulationRA4/ To explore the proportion of patients treated with H2RA suffering from renal impairment

Study Design

Non-interventional study design
Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code
(A02BA) H2-receptor antagonists

Population studied

Short description of the study population
The study population consisted of all persons with observation time during the study period. Subjects were included in the study if they contributed active follow-up time during the study period. No other inclusion or exclusion criteria were applied.

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)

Special population of interest
Renal impaired

Estimated number of subjects
1300000

Study design details

Data analysis plan
All results will be presented by database. Results pooled over the different databases will be provided for the indication of use and history of renal impairment. Drug use both for prevalent and incident users will be expressed as the number of users per 1,000 persons presented by calendar year, age category (10 years), formulation and sex. Per patient, the cumulative duration will be calculated which is the sum of the duration of the Drug Eras per H2RA ingredient. Results on cumulative duration will be presented as median (and corresponding Q1, Q3, P5, P95, min, max) by class and type of H2RA ingredient, stratified by age category at start, gender and also by formulation (oral or parenteral).Results on PDD/DDD ratio and cumulative exposure (=cumulative number of DDDs) will be presented as median (and corresponding Q1, Q3, P5, P95, min, max) by type of H2RA and stratified by age category, gender, and formulation

Documents

Study results
Rantidine_finalreport_7thapril2020.pdf(3.49 MB)

Data management

Data sources

Data source(s)
THIN® (The Health Improvement Network®)
IPCI

The Information System for Research in Primary Care (SIDIAP)

Data source(s), other
THIN, IPCI, SIDIAP, IMS LifeLink:Longitudinal Prescription Data - Bel, DA France, DA Germany

Data sources (types)
Administrative data (e.g. claims)
Electronic healthcare records (EHR)

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