Study of exposure and use patterns of alternatives to ranitidine-containing medicines in patients treated with ranitidine (Ranitidine)

First published: 02/12/2021

Last updated: 12/06/2024

Study Finalised

Administrative details

EU PAS number

EUPAS44548

Study ID

44568

DARWIN EU® study

No

Study countries

- ☐ Belgium
- ☐ France
- ☐ Germany

☐ Netherlands

☐ Spain

☐ United Kingdom

Study description

Ranitidine is a competitive and reversible inhibitor of the action of histamine and indicated for the management of peptic ulceration (with or without Helicobacter Pylori), Gastro-Esophageal Reflux Disease (GERD), reflux oesophagitis and Zollinger-Ellison syndrome. In 2019, results of a preliminary laboratory analysis have shown the presence of N-Nitrosodimethylamine (NDMA), a human carcinogen, in ranitidine. Many ranitidine-containing medicines have not been available in the EU for several months since the initiation of the referral, because national competent authorities have recalled them either due to levels of NDMA found in the products or as a precaution while the EMA review is ongoing. Healthcare professionals have been asked to advise patients on alternative medicines. In addition, in some Member States the outcome of the referral was communicated at national level through media campaigns, involving learned societies and medical associations to inform prescribing physicians and health care organisations about these changes. The unavailability of ranitidine-containing medicines is expected to cause patients to switch treatment to alternative medicines or alternative treatment strategies. The extent of switches to alternative medicines remains unknown as well as the rate of patients permanently discontinuing treatment following unavailability of ranitidine-containing medicines. The overall aim of this study is to evaluate the impact of the regulatory actions taken for ranitidine containing medicinal products following the 2019 referral procedure, using healthcare databases of six European countries. Data from these databases have been mapped to the OMOP Common Data Model.

Study status

Finalised

Research institutions and networks

Institutions

IQVIA NL, Real-World-Evidence

Netherlands

First published: 25/11/2022

Last updated: 21/03/2025

Institution | Other | 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: 23/05/2025

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

Multiple centres: 6 centres are involved in the study, Erasmus University Rotterdam

Contact details

Study institution contact

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Primary lead investigator

Katia Verhamme

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 27/10/2019

Actual: 27/10/2020

Study start date

Planned: 01/09/2017

Actual: 01/09/2017

Data analysis start date

Planned: 01/09/2017

Actual: 01/09/2017

Date of final study report

Planned: 28/04/2023

Actual: 28/04/2023

Sources of funding

- EMA

Study protocol

ranitidine protocol_16thseptember2021_clean.pdf(2.14 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:

Disease /health condition

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Drug utilisation

Data collection methods:

Secondary use of data

Main study objective:

To determine drug utilisation and prescription patterns of medicinal products containing ranitidine (A02BA02) and alternative medicinal products (other H2 receptor antagonists, proton pump inhibitors and other medicinal products for acid-related disorders).

Study Design

Non-interventional study design

Cohort

Other

Non-interventional study design, other

Retrospective population-based study

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(A02BA01) cimetidine

cimetidine

(A02BA02) ranitidine

ranitidine

(A02BA04) nizatidine

nizatidine

(A02BA06) roxatidine

roxatidine

(A02BA08) lafutidine

lafutidine

(A02BA51) cimetidine, combinations

cimetidine, combinations

Medical condition to be studied

Peptic ulcer

Additional medical condition(s)

Incidence of use of ranitidine and alternatives medicines to ranitidine (other H2RA, PPIs, antacids and other drugs used for peptic ulcer and GERD) Treatment discontinuation in patients treated with ranitidine Switching from ranitidine to alternative medicines

Population studied

Short description of the study population

The study population included all individuals exposed to ranitidine-containing medicines identified from six databases from six European countries namely IPCI (the Netherlands), SIDIAP (Catalonia Spain) and IQVIA (UK IMRD, LPD Belgium, DA Germany and LPD France) for the period of 1st January 2017 until 1st January 2023.

Age groups

Preterm newborn infants (0 – 27 days)

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)

Estimated number of subjects

1250000

Study design details

Outcomes

Incidence of use of ranitidine and alternatives medicines to ranitidine (other H2RA, PPIs, antacids and other drugs used for peptic ulcer and GERD) Treatment discontinuation in patients treated with ranitidine Switching from ranitidine to alternative medicines

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Data analysis plan

An initial exploratory analysis will be conducted for each country-specific cohort to summarise baseline demographic characteristics, medical conditions at time of treatment initiation, indication and exposure. Incident drug use will be expressed as the number of users per 1,000 persons per quarter, calendar year and by referral period. For each database (and thus by country), stratum specific estimates will be presented separately according to: referral period (pre-, during- and post-referral), indication, age category, sex and formulation.

Documents

Study results

Ranitidine report_30 March 2023_clean.pdf(2.64 MB)

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)

Integrated Primary Care Information (IPCI)

IQVIA Disease Analyzer Germany

IQVIA Longitudinal Patient Data - Belgium

The Information System for Research in Primary Care (SIDIAP)

IQVIA Medical Research Data - OMOP

Longitudinal Patient Data - France

Data sources (types)

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