Post-marketing Surveillance Study of the Effectiveness and Safety of new Oral Antivirals for outpatients with mild-moderate COVID-19. (ESOA-19)

First published: 18/07/2022

Last updated: 05/06/2025

Study | Planned

Administrative details

EU PAS number

EUPAS48186

Study ID

49575

DARWIN EU® study

No

Study countries

Portugal

Study description

There is an increased lack of short- and long-term real-life effectiveness and safety data on new oral antivirals authorised and commercialised to treat COVID-19.
To date, only two clinical trials have been published with data on the efficacy and safety of the use of the Paxlovid® and Lagevrio®.
Since there is a public health, political, social and economic pressure to prevent severity, hospitalisation and death from COVID-19, monitoring the effectiveness and safety of commercialised oral antiviral therapies against COVID-19 has become emergent pharmacovigilance and public health task.
The objective of the study is to monitor the post-marketing safety and effectiveness of the new oral antivirals indicated for the treatment of COVID-19, namely Nirmatrelvir/Ritonavir (Paxlovid®) and Molnupiravir (Lagevrio®), having as holders of the Authorization of Market introduction to Pfizer Europe MA EEIG and Merck Sharp & Dohme B.V., respectively.

Study status

Planned

Research institutions and networks

Institutions

Porto Pharmacovigilance Centre, Faculty of Medicine, University of Porto (UFPorto)

Portugal

First published: 17/11/2010

Last updated: 12/06/2023

Institution | Educational Institution | ENCePP partner

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Renato Ferreira da Silva

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 11/07/2022

Actual: 11/07/2022

Study start date

Planned: 01/08/2022

Data analysis start date

Planned: 01/09/2022

Date of interim report, if expected

Planned: 30/06/2024

Date of final study report

Planned: 25/04/2025

Sources of funding

- EU institutional research programme

More details on funding

Portuguese national funds and Community funds from the European Social Fund (ESF) through FCT – Fundação para a Ciência e a Tecnologia (Portugal)).

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 type:

Non-interventional study

Scope of the study:

Assessment of risk minimisation measure implementation or effectiveness

Drug utilisation

Effectiveness study (incl. comparative)

Main study objective:

To generate real-world evidence on the effectiveness and safety of COVID-19 oral antiviral medicines, therefore contributing to support informed political, regulatory and clinical decisions.

Study Design

Non-interventional study design

Cohort

Other

Non-interventional study design, other

Prescription event monitoring

Study drug and medical condition

Medicinal product name

PAXLOVID

LAGEVRIO

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

NIRMATRELVIR

RITONAVIR

Anatomical Therapeutic Chemical (ATC) code

(J05AE30) nirmatrelvir and ritonavir

nirmatrelvir and ritonavir

Medical condition to be studied

COVID-19

Population studied

Age groups

- 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

Hepatic impaired

Immunocompromised

Renal impaired

Estimated number of subjects

107

Study design details

Outcomes

Safety outcomes: the incidence of AE (with particular focus on AE of special interest) that emerge during or after the treatment period, serious AE, and AE leading to discontinuation of the treatment, as coded according to the MedDRA. Effectiveness outcomes: the incidence of hospitalisation for any cause (defined as ≥24 hours of acute care in a hospital or any similar facility) or death for any, Adherence to treatment: will be measured using the self-reported 7-item

Measure Treatment Adherence (MTA) tool validated for the Portuguese Population9.
The MTA is a psychometric tool derived from the Morisky et al. questionnaire and evaluates the individuals` behavior concerning the daily use of medication.

Data analysis plan

A descriptive analysis will be conducted on all study variables.
Categorical variables will be described through absolute and relative frequencies, and continuous variables will be described by descriptive statistics using mean and standard deviation, quartiles, median value, and minimum and maximum values.
Demographic and screening data will be described using the descriptive measures defined above and according to each variable type. Clinical information recorded at baseline visit will also be described to all subjects
Univariate and multivariate regression analyses will be performed to evaluate the relationship between the presence of risk factors and AE.
Survival analysis will be conducted for time until hospitalization and until dead (total and medicines related) and until AE. A propensity score model will be applied to compare the safety and effectiveness of the different oral antivirals.

Summary results

Molnupiravir cohort: By day 29 post-treatment initiation, no deaths were reported (n = 0; 0%; 95%CI = [0,26]), and all patients were either at home or institutionalised, with favourable outcomes.
Out of the 12 patients enrolled, eight (67%; 95%CI = [35,90]) reported at least one AE, with the median time to the first AE being five days (range 5–7 days). Half of the patients (n = 6; 95%CI = [21,79]) reported AE deemed possibly or probably related to molnupiravir, involving nausea (25%), dizziness (17%), bitter taste (17%), and headache (17%).
These AE were more commonly observed in older individuals and those

overweight, indicating a potential influence of these factors on AE occurrence. Molnupiravir appears to show good safety and effectiveness, offering an alternative for high-risk COVID-19 outpatients ineligible for first-line therapy. Despite its market withdrawal, ongoing research into its long-term effects is crucial to potentially repurpose it for other viral infections.

Documents

Study results

s43440-025-00729.pdf (1.16 MB)

Study publications

https://link.springer.com/article/10.1007/s43440-025-00729-2

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

EUPAS48186-48194.pdf (160.73 KB)

Composition of steering group and observers

Composition of Steering Group and Observers_signed.pdf (400.67 KB)

Data sources

Data source(s), other

Drug prescriptions; Pharmacy dispensing records

Data sources (types)

Other

Data sources (types), other

Prospective patient-based data collection, prescription event monitoring

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