# 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





## Administrative details

**Study description** 

EU PAS number	
EUPAS48186	
Study ID	
49575	
DARWIN EU® study	
No	
Study countries	
Portugal	

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	
<b>Last updated:</b> 12/06/2023	
Institution	

## 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

#### Name of medicine

**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

# 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