

# 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

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### Study ID

49575

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### DARWIN EU® study

No

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### Study countries

 Portugal

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### 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.

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## 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

[renato.ivos@gmail.com](mailto:renato.ivos@gmail.com)

### 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

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### Study start date

Planned: 01/08/2022

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### Data analysis start date

Planned: 01/09/2022

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### Date of interim report, if expected

Planned: 30/06/2024

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### 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

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### **Is the study required by a Risk Management Plan (RMP)?**

Not applicable

## Methodological aspects

### Study type

### Study type list

#### **Study type:**

Non-interventional study

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#### **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

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**Non-interventional study design, other**

Prescription event monitoring

## Study drug and medical condition

**Medicinal product name**

PAXLOVID

LAGEVRIO

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

NIRMATRELVIR

RITONAVIR

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**Anatomical Therapeutic Chemical (ATC) code**

(J05AE30) nirmatrelvir and ritonavir

nirmatrelvir and ritonavir

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**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)
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### Special population of interest

Hepatic impaired

Immunocompromised

Renal impaired

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### 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  $\geq 24$  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 Population<sup>9</sup>.

The MTA is a psychometric tool derived from the Morisky et al. questionnaire and evaluates the individuals' behavior concerning the daily use of medication.

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### **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 death (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.

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### **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)

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### Study publications

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

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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

[EUPAS48186-48194.pdf](#) (160.73 KB)

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### Composition of steering group and observers

## Data sources

### Data source(s), other

Drug prescriptions; Pharmacy dispensing records

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### Data sources (types)

Other

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### 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

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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