# Cost-effectiveness of nirmatrelvir/ritonavir for the treatment of outpatient SARS-CoV-2 in adult patients at risk for developing severe disease in Greece

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## INTRODUCTION

- Coronavirus disease 2019 (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has been one of the greatest threats to public health in the 21st century[1]. As of September 2023, there were over 6.9 million deaths globally from COVID-19, while Greece alone has seen over 37 thousand deaths[2].

- This public health threat has persisted to this day, despite the several modifications of the virus. COVID-19 exerts a high clinical burden on patients and healthcare systems worldwide, which may persist for a long period of time[3,4]. As of 8 October 2023, the hospital admission rate among 18 EU/EEA countries was 1.8 per 100,000 people.[5]

- These lead to significant healthcare service disruptions and high healthcare resource utilization, associated with increased humanistic and economic burden[6,7]. The future state of COVID-19 is highly dependent on viral evolution, population immunity, and access, affordability, and use of life-saving tools[6]. Antiviral treatment is a critical and complementary tool, along with vaccines, to reduce the risk of progression to severe illness.

- Nirmatrelvir/ritonavir is the only orally administered EMA approved antiviral for the treatment of COVID-19 in adults who do not require supplemental oxygen and who are at increased risk for progressing to severe COVID-19[8]. Results from EPIC-HR trial* demonstrated that nirmatrelvir/ ritonavir significantly reduced the risk of hospitalization and death from COVID-19 compared with placebo[9,10] The value of nirmatrelvir/ ritonavir has been recognized by the medical community as it is the recommended first-line treatment by WHO[11], US[3] and Greek[12] clinical guidelines for high-risk patients.

## OBJECTIVE

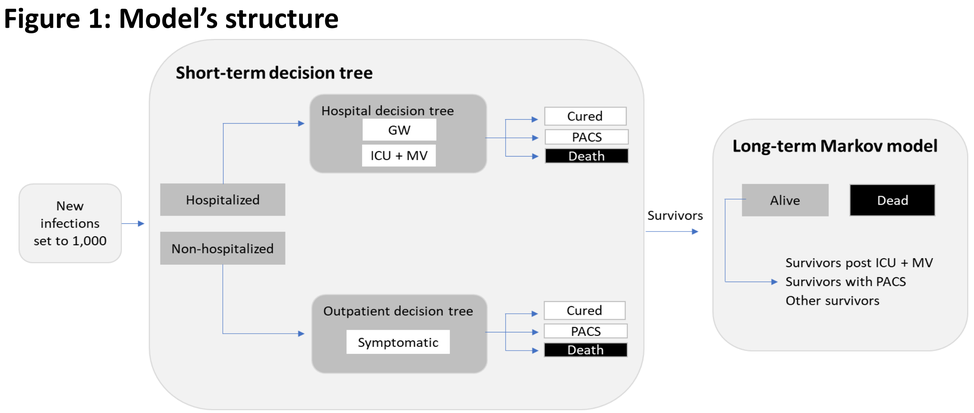
- The present study was conducted to assess the health and economic impact, associated with the introduction of nirmatrelvir/ritonavir for the treatment of COVID-19 for adults who do not require supplemental oxygen and who are at increased risk for progressing to severe COVID-19 in Greece.

## METHODS

- A pharmacoeconomic model was used to estimate the implications of COVID-19 patients in the Greek setting.

- **Structure:** the model comprises of a timed decision tree spanned over a one-year period, to evaluate short-term implications of infected patients, followed by a Markov lifetime model. Individuals were associated with levels of care (non-hospitalization, hospitalisation in General Ward-GW and in Intensive Care Unit-ICU). Survivors of the short-term module entered the lifetime module which consisted of a Markov model (Figure 1).

**Figure 1: Model's structure**




- **Population:** nirmatrelvir/ritonavir was compared to standard of care (no anti-SARS-CoV-2 treatment in outpatient setting). Target population are adult patients with confirmed COVID-19 at risk for developing severe disease, aligned with the population of the EPIC-HR trial. A closed cohort of 1,000 infected individuals was evaluated, and population characteristics were derived by EPIC-HR trial (Table 1).

- **Discounting and willingness-to-pay (WTP) threshold:** Costs and QALYs were discounted with a 3.5% rate. While there is no official WTP threshold in Greece, a WTP threshold of €30,000 per QALY was considered in this analysis, to align with health technology assessment guidance in Europe and with WHO recommendation[13,14]. COVID-related costs were collected from official and publicly available sources (Table 1).

- **Sensitivity analysis:** the robustness of the model was evaluated using one-way (DSA) and probabilistic sensitivity (PSA) analyses, where key model parameters, such as proportion of vaccinated patients and hospitalization cost, were varied.

**Table 1: Effectiveness and cost parameters**

| Treatment efficacy parameters | Value | Source/Notes |
|---|---|---|
| **Nirmatrelvir/ritonavir** | | |
| Reduction in infection length | 20.0% | EPIC HR[10] |
| Reduction of hospitalisations | 85.8% | EPIC HR[10] |
| Reduction in deaths | 85.8% | EPIC HR[10] |

| Direct cost parameters | Cost | Source/Notes |
|---|---|---|
| **Outpatient healthcare costs** | | |
| Practitioner's office | 10 € | Government Gazette 458 τ.Β΄/25-2-2014[15] |
| Extended care facility stay | 80 € | Government Gazette 2150-27 September 2011[16] |
| **Hospitalisation healthcare costs** | | |
| GW | 1,401 € | |
| ICU/no MV | 3,773 € | Government Gazette 946/2012[17] |
| ICU/MV | 5,281 € | |
| Average cost per PACS/Long COVID-19 case | 1,401 € | Average readmission rate, estimated hospital stay conservative estimate same as GW |

## RESULTS

- Nirmatrelvir/ritonavir is considered to be a dominant (more effective, less costly) strategy over standard of care (non-antiviral treatment) for treating adult outpatients with confirmed COVID-19 in Greece and leads to cost-savings for the public payer.

- One year time horizon analysis revealed that treatment with nirmatrelvir/ritonavir is a cost saving strategy with a cost difference of -42.70 € and 0.002 incremental QALY per capita and indicates that nirmatrelvir/ritonavir is dominant over SoC, with a net monetary benefit of 112.08 €. Lifetime analysis results to a cost difference of -42,702 € and 18 QALYs (Table 2).

**Table 2: Results**

| **Short term outcomes** | | | |
|---|---|---|---|
| **Per capita** | | | |
| | **Intervention** | **Comparator** | **Difference** |
| Total cost | 1,350.47 € | 1,393.17 € | -42.70 € |
| Total QALYs | 0.788 | 0.785 | 0.002 |
| **Cost per QALY** | | | Dominant |
| **Net monetary benefit** | | | 112.08 € |
| | | | |
| **Lifetime outcomes** | | | |
| **1000 infected patients** | **Intervention** | **Comparator** | **Difference** |
| Lifetime costs | 1,350,471 € | 1,393,172 € | -42,702 € |
| QALY | 17,254 | 17,236 | 18 |
| **Per capita** | **Intervention** | **Comparator** | **Difference** |
| Lifetime costs | 1,350 € | 1,393 € | -43 € |
| QALY | 17.25 | 17.24 | 0.018 |
| | | | |
| **Cost per QALY** | | | Dominant |
| **Net monetary benefit** | | | 575.53 € |

- DSA indicates that ICER was most sensitive to the proportion vaccinated in high risk and hospitalization cost (general ward). The top 20 most influential parameters are shown in the tornado plot for the ICERs ranked from most to least influential (Figure 1). There is a high degree of certainty around the mean value results (Figure 2).

**Figure 1: ICER tornado plot from the DSA using a 10% variation from the mean (per capita, over a short-term time horizon)**

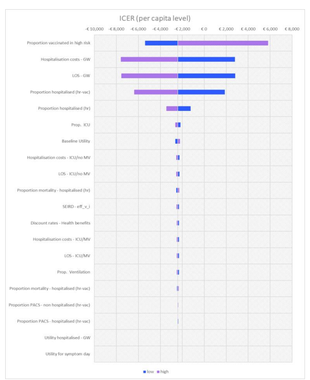



**Figure 2: ICER scatter plot from the PSA (per capita, over a short-term time horizon)**


## CONCLUSIONS

- Nirmatrelvir/ritonavir is considered to be a dominant (more effective, less costly) strategy over standard of care for the treatment of COVID-19 for adults who do not require supplemental oxygen and who are at increased risk for progressing to severe COVID-19 in Greece and leads to cost-savings for the public payer.

- The results of this analysis highlight the value of nirmatrelvir/ritonavir as a treatment strategy for Greek patients with increased risk for progressing to severe COVID-19 and could be used to inform decision makers about the benefit of nirmatrelvir/ritonavir in the Greek healthcare setting.

## DISCLOSURES

This study was funded by Pfizer Hellas. OZ, MB, VG, AR, AL are employees of Pfizer Hellas. MK is an employee of IQVIA Hellas, which was a paid consultant to Pfizer in connection with the development of this study.

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Notes:

* phase 2/3 Evaluation of Protease Inhibitor for COVID-19 in High Risk patients, randomised, double-blind, placebo-controlled study, NCT04960202

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