WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.453
Volume 14, Issue 19, 663-676. Research Article ISSN 2277–7105

NIRMATRELVIR IN COVID-19 THERAPY: "TARGETING SARS-CoV-2 MAIN PROTEASE"

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Article Received on
12 August 2025,

Revised on 01 Sept. 2025,
Accepted on 21 Sept. 2025

https://doi.org/10.5281/zenodo.17221853

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ABSTRACT

Nirmatrelvir, a potent orally bioavailable 3C-like protease (3CL^pro) inhibitor, represents a significant advancement in the management of COVID-19. Co-administered with ritonavir as Paxlovid, it maintains optimal plasma concentrations by inhibiting CYP3A-mediated metabolism, thereby enhancing antiviral efficacy. Nirmatrelvir prevents viral replication by blocking proteolytic cleavage of SARS-CoV-2 polyproteins, a crucial step in viral maturation. Clinical trials such as EPIC-HR have demonstrated an 88% reduction in hospitalization or death among high-risk, non-hospitalized patients with mild-to-moderate COVID-19 when therapy is initiated within five days of symptom onset. Although generally well tolerated, reported adverse effects include dysgeusia, diarrhoea, and potential drug–drug interactions due to ritonavir's strong CYP3A inhibition. Regulatory approvals worldwide and its oral route of administration make nirmatrelvir a valuable option for outpatient COVID-19 therapy, enabling early intervention and reducing healthcare burden. Ongoing research explores its role in preventing long COVID and addressing emerging SARS-CoV-2 variants.

KEYWORDS: Nirmatrelvir, Ritonavir, Paxlovid, COVID-19, SARS-CoV-2, 3CL protease inhibitor, antiviral therapy, EPIC-HR trial.

INTRODUCTION

Since the emergence of coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), multiple strategies have been explored to develop effective antiviral therapies.[1] Early efforts primarily focused on repurposing existing drugs with known antimicrobial or antiviral activity, including hydroxychloroquine

(with or without azithromycin), favipiravir, and nelfinavir. However, large-scale clinical trials demonstrated that these agents were ineffective in inhibiting SARS-CoV-2 replication or improving clinical outcomes. Consequently, attention shifted toward the discovery and development of novel antivirals targeting key steps in the viral life cycle.[2]

Among the candidates, remdesivir, a broad-spectrum RNA polymerase inhibitor, and molnupiravir, a nucleoside analog that induces viral RNA chain termination, showed promise. In parallel, several monoclonal antibodies targeting the SARS-CoV-2 spike protein were granted emergency use authorization but later withdrawn due to reduced efficacy against emerging variants.[3]

Nirmatrelvir (PF-07321332), a potent and selective oral inhibitor of the SARS-CoV-2 main protease (3CL^pro), was rapidly developed in response to the pandemic. When co-administered with ritonavir, a pharmacokinetic enhancer, the combination is marketed as PAXLOVID™ (Pfizer Inc., New York, NY). This therapy is approved for treating mild-to-moderate COVID-19 in adults at high risk of progression to severe disease. Phase 2/3 clinical trials demonstrated that nirmatrelvir/ritonavir significantly reduced the risk of hospitalization or death by approximately 86% compared with placebo when administered early.[4] This review aims to summarize the clinical pharmacology, pharmacokinetics, and therapeutic relevance of nirmatrelvir/ritonavir and highlight its impact on COVID-19 management.

Fig.1 Chemical Structure of nirmatrelvir

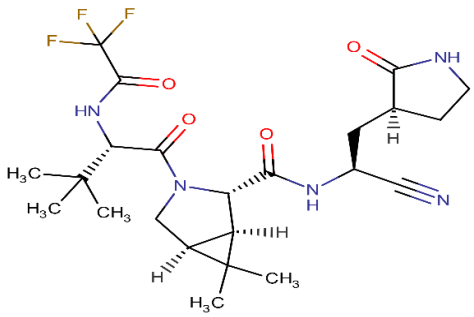

Figure 1: Chemical structure of Nirmatrelvir, a 3CL^pro inhibitor that blocks SARS-CoV-2 replication.

IUPAC Name

(1*R*,2*S*,5*S*)-*N*-[(1*S*)-1-cyano-2-[(3*S*)-2-oxopyrrolidin-3-yl] ethyl]-3-[(2*S*)-3,3-dimethyl-2-[(2,2,2-trifluoroacetyl) amino] butanoyl]-6,6-dimethyl-3-azabicyclo hexane-2-carboxamide

Chemical Formula

$C_{23}H_{32}F_3N_5O_4$

Molecular weight - 499.535 gm.mol^{-1}

Melting Range - 192.9 °C (379.2 °F)

Solubility

Table 1: Solubility profile of Nirmatrelvir in different media.

Solubility (25°C)*	In vitro	DMSO	100 mg/mL (200.18 mM)
		Ethanol	100 mg/mL (200.18 mM)
		Water	2 mg/mL (4.0 mM)

Table 1. Solubility profile of nirmatrelvir in different media (table 1) summarizes the solubility of nirmatrelvir in various solvents. Such data are essential for understanding its oral bioavailability and formulation considerations. Higher solubility in aqueous and physiologically relevant media supports its effectiveness as an oral therapeutic agent.

Background

Nirmatrelvir is an orally bioavailable 3C-like protease (3CL^{PRO}) inhibitor that is the subject of clinical trial NCT04756531. 3CL^{PRO} is responsible for cleaving polyproteins 1a and 1ab of SARS-CoV-2.[5] Without the activity of the SARS-CoV-2 3CL^{PRO}, non-structural proteins (including proteases) cannot be released to perform their functions, inhibiting viral replication.[6]

In 2020, Pfizer was investigating another potential treatment for SARS-CoV-2. Both drugs were inhibitors of SARS-CoV-2 3CL^{PRO}, but nirmatrelvir has the advantage of being orally bioavailable.[7] Nirmatrelvir is advantageous in that it can be prescribed to patients before they require hospitalization, while requires intravenous administration in hospital. In December 2021, the FDA granted an emergency use authorization to Paxlovid, a copackaged product containing both nirmatrelvir and ritonavir, for the treatment of certain patients with mild-to-moderate COVID-19.[8] It was fully approved by the FDA on May 25, 2023. Paxlovid was approved for use in Canada in January 2022 for the treatment of adult patients

with mild-moderate COVID-19 and later granted conditional marketing authorization by the European Commission on January 27, 2022.[7]

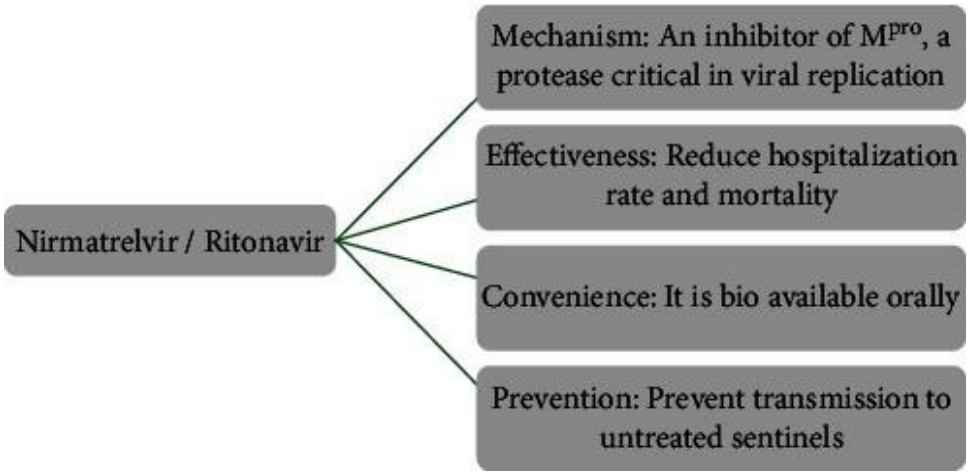

Fig. 2: Key benefits of Nirmatrelvir/Ritonavir (Paxlovid) in COVID-19 Management.

Fig. 2 Key benefits of Nirmatrelvir/Ritonavir (Paxlovid) in COVID-19 Management (fig.2) This figure highlights the major advantages of nirmatrelvir/ritonavir therapy, including its oral bioavailability and ease of use, its effectiveness in reducing hospitalization and mortality rates, and its role in preventing transmission when given early.

History

Nirmatrelvir belongs to a family of 3C-like protease inhibitors developed in the late 2010s against feline coronavirus while ritonavir is an antiretroviral drug invented in the 1980s and used since the 1990s to inhibit the enzyme that metabolizes other protease inhibitors.[9] The primary data supporting the US Food and Drug Administration (FDA) emergency use authorization for nirmatrelvir/ritonavir were from the EPIC-HR trial, a randomized, double-blind, placebo-controlled clinical trial studying nirmatrelvir/ritonavir for the treatment of non-hospitalized symptomatic adults with a laboratory confirmed diagnosis of SARS-CoV-2 infection. Participants were adults 18 years of age and older with a prespecified risk factor for progression to severe disease or were 60 years and older regardless of prespecified chronic medical conditions.[10] All participants had not received a COVID-19 vaccine and had not been previously infected with COVID-19. The main outcome measured in the trial was the proportion of people who were hospitalized due to COVID-19 or died due to any cause during 28 days of follow-up. EPIC-HR started in July 2021, and completed in December 2021.[11]

Nirmatrelvir/ritonavir significantly reduced the proportion of people with COVID-19 related hospitalization or death from any cause by 88% compared to placebo among participants treated within five days of symptom onset and who did not receive COVID-19 therapeutic monoclonal antibody treatment. On 14 December 2021, Pfizer also announced that a Phase II/III study of nirmatrelvir/ritonavir showed a reduced risk of hospitalization or death. In August 2021, Pfizer began a phase II/III trial of nirmatrelvir/ritonavir for COVID-19 in standard-risk individuals with COVID-19 known as EPIC-SR. Interim results of this trial were announced in December 2021, and final results were released in June 2022. The study did not find a statistically significant reduction in the risk of hospitalization, death, or sustained alleviation of symptoms, although there was a significant decrease in COVID-19-related medical visits. Pfizer discontinued enrolment in the study with the reason given being the very low rate of hospitalization and death in this population. In December 2021, nirmatrelvir/ritonavir was granted emergency use authorization by the United States Food and Drug Administration (FDA) for the treatment of COVID-19.[12] On 31 December, the United Kingdom's Medicines and Healthcare products Regulatory Agency (MHRA) approved the use of nirmatrelvir combined with ritonavir for adults with mild to moderate infection and at high risk of their illness worsening. In April 2022, it was announced that the PANORAMIC trial would start testing the effectiveness of nirmatrelvir/ritonavir for treating COVID-19 infections. Nirmatrelvir/ritonavir has been evaluated in the treatment of COVID-19 in standard-risk individuals in the EPIC-SR trial. This study did not achieve its primary goal of reducing time to sustained alleviation of COVID-19 symptoms (treatment: 13 days (95% CI 12–15 days); placebo: 13 days (95% CI 11–14 days)). It also did not find a statistically significant reduction in the risk of hospitalization or death (treatment: 5/576 [0.9%]; placebo: 10/569 [1.8%]; $p > 0.05$). Likewise, findings were not statistically significant for reducing hospitalization rates in a subgroup of vaccinated adults with at least one risk factor for severe COVID-19 (treatment: 3/361 [0.8%]; placebo: 7/360 [1.9%]; 57% reduction – RR 0.43, 95% CI 0.11–1.64). However, the trial did find a statistically significant 62% decrease in COVID-19-related medical visits, similar to the 67% reduction from the EPIC-HR study of high-risk individuals. Enrolment in EPIC-SR was discontinued due to the low rate of hospitalization and death in this population. In May 2023, nirmatrelvir/ritonavir was approved for medical use in the United States for the treatment of mild-to-moderate COVID-19 in adults who are at high risk for progression to severe COVID-19, including hospitalization or death.[13]

Table 2: Physiochemical properties of Nirmatrelvir.

XLogP3-AA	2.2
Hydrogen Bond Donor Count	3
Hydrogen Bond Acceptor Count	8
Rotatable Bond Count	7
Exact Mass	499.24063901 g/mol
Monoisotopic Mass	499.24063901 g/mol
Topological Polar Surface Area	131Å²
Heavy Atom Count	35
Formal Charge	0
Complexity	964
Isotope Atom Count	0
Defined Atom Stereocenter Count	6
Undefined Atom Stereocenter Count	0
Defined Bond Stereocenter Count	0
Undefined Bond Stereocenter Count	0
Covalently-Bonded Unit Count	1
Compound Is Canonicalized	Yes

Table 2. Physiochemical properties of nirmatrelvir (table 2) summarizes key physicochemical properties of nirmatrelvir, which support its oral bioavailability, stability, and suitability as a 3CL^pro inhibitor for COVID-19 therapy.

Pharmacokinetics

Table 3: Pharmacokinetic Profile of Nirmatrelvir (with ritonavir).

Parameter	Description/Observation
Primary PK parameters	Cmax (Maximum plasma concentration), AUCinf (Area under the plasma concentration–time curve extrapolated to infinity), % unchanged drug excreted in urine over 48 h, Renal clearance (CLr).
Secondary PK parameters	Plasma concentration at 12 h, Tmax (Time to reach Cmax), AUClast (AUC up to last measurable concentration), Apparent clearance (CL/F), Apparent volume of distribution, Terminal elimination half-life (t1/2).
Sample collection	Blood samples (~4 mL) collected at 0, 0.5, 1, 2, 3, 4, 6, 8, 10, 12, 24, 36, and 48 h post-dose. Urine samples collected in ≤24 h and >24–48 h intervals.
Metabolism	Primarily metabolized by CYP3A4. Co-administration with ritonavir (CYP3A4 inhibitor) maintains therapeutic plasma concentrations.
PK analysis method	Parameters calculated using non-compartmental analysis (oNCA proprietary program).

Table 3. Pharmacokinetic profile of nirmatrelvir (table 3) gives summary of key pharmacokinetic parameters, sampling strategy, and metabolism of nirmatrelvir with ritonavir.[4]

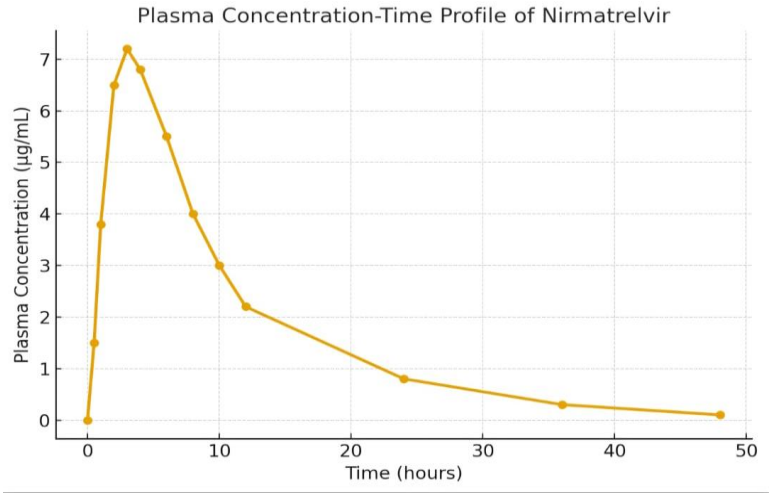

Fig. 3; Concentration-time profile curve.

Fig.3 concentration-time profile curve (fig.3) Plasma concentration–time profile of nirmatrelvir following oral administration with ritonavir, showing rapid absorption (Cmax within 2–3 h) followed by gradual elimination over 48 h.

Mechanism of action

Nirmatrelvir is an inhibitor of a cysteine residue in the 3C-like protease ($3CL^{PRO}$) of SARS-CoV-2. This cysteine is responsible to the activity of the $3CL^{PRO}$ of SARS-CoV-2 and potentially other members of the coronavirus family. The $3CL^{PRO}$, also known as the main protease or non-structural protein 5, is responsible for cleaving polyproteins 1a and 1ab. These polyproteins contain the $3CL^{PRO}$ itself, a papain-like (PL) cysteine protease, and 14 other non-structural proteins. Without the activity of the $3CL^{PRO}$, non-structural proteins (including proteases) cannot be released to perform their functions, inhibiting viral replication.[14]

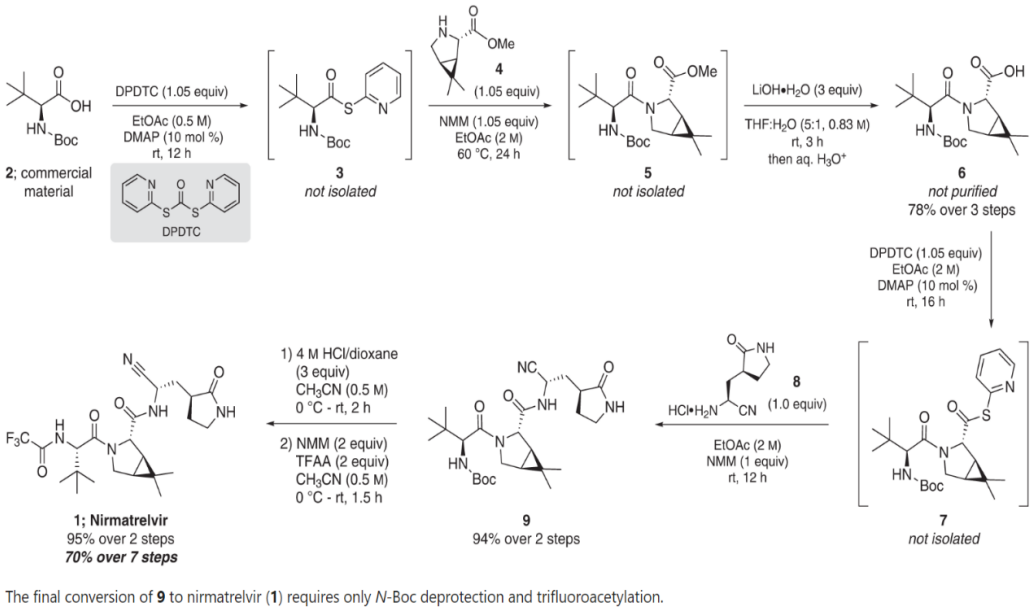

Fig. 4: Mechanism of action of Nirmatrelvir.

Fig. 4 Mechanism of action of Nirmatrelvir (fig.4) Nirmatrelvir inhibits SARS-CoV-2 3CLpro preventing polyprotein cleavage and halting viral replication.

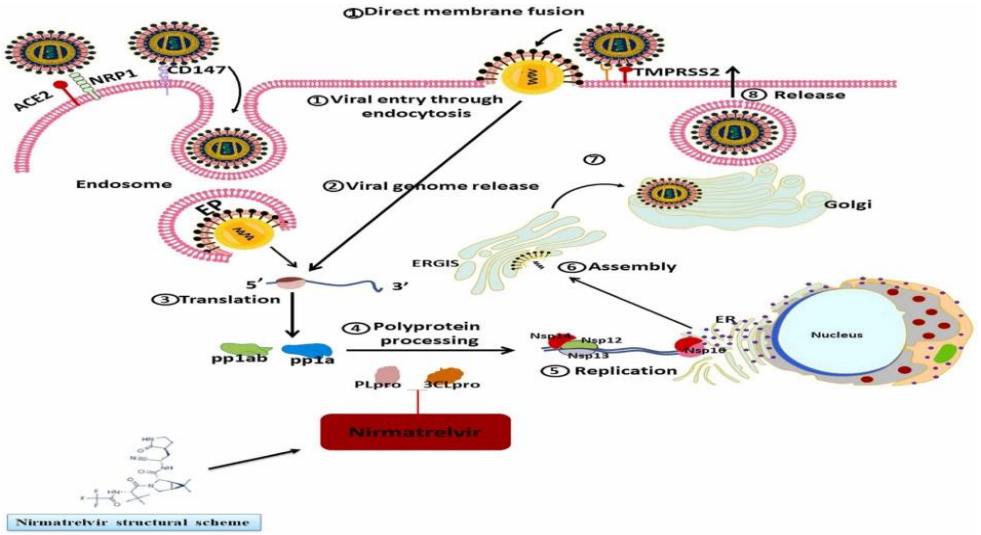

Fig. 5: The mechanism of action of Nirmatrelvir in inhibiting SARS-CoV-2 replication, specifically targeting the viral 3CLpro enzyme.

Fig. 5 The mechanism of action of Nirmatrelvir in inhibiting SARS-CoV-2 replication, specifically targeting the viral 3CLpro enzyme (fig.5) The diagram shows two main pathways for viral entry: direct membrane fusion and viral entry through endocytosis, both involving interaction with ACE2 and other host factors.

Uses

(i) Treatment for COVID-19

Nirmatrelvir and ritonavir are used to treat mild-to-moderate COVID-19 in people who are highly susceptible to serious illness, hospitalisation, or death.[15]

(ii) Prevention of Severe Disease

This combination lowers the risk of hospitalisation by preventing the disease from progressing to severe stages by blocking SARS-CoV-2 replication.[16]

(iii) Outpatient Management

Because Paxlovid is intended to be taken orally, it can be treated outside of a hospital, allowing for early intervention before symptoms worsen.[17]

(iv) High-Risk Populations

Those who are older, unvaccinated, or have pre-existing medical illnesses including diabetes, heart disease, or obesity—who are more likely to experience complications from COVID-19—benefit greatly from it.[11]

Adverse effects

Changes in taste or diarrhoea may occur. If either of these effects lasts or gets worse, tell your doctor or pharmacist promptly. Tell your doctor right away if you have any serious side effects, including: signs of liver problems (such as nausea/vomiting that doesn't stop, loss of appetite, stomach/abdominal pain, yellowing eyes/skin, dark urine).[2]

A very serious allergic reaction to this drug is rare. However, get medical help right away if you notice any symptoms of a serious allergic reaction, including: rash, itching/swelling (especially of the face/tongue/throat), severe dizziness, trouble breathing. This is not a complete list of possible side effects. If you notice other effects not listed above, contact your doctor or pharmacist.[15]

As nirmatrelvir is an investigational drug, there is limited clinical data about its potential adverse effects. However, data from the EPIC-HR trial suggests that it is generally well-tolerated by patients with COVID-19. The most common adverse effects include dysgeusia, diarrhoea, hypertension, and myalgia. In addition, hypersensitivity reactions, which may manifest as urticaria, angioedema, pruritus, and dyspnoea, have been reported. Cases of anaphylaxis, Stevens-Johnson syndrome, and toxic epidermal necrolysis have also been

reported with ritonavir use. Hyperlipidaemia, hypertriglyceridemia, and other metabolic adverse effects have also been noted with ritonavir.[18]

Hepatic transaminase elevations have been reported, but transaminase elevations have also been attributed to COVID-19(A confounding factor). The risk of hepatotoxicity is low, and the Likelihood score is E:(unlikely cause of clinically apparent liver injury).[19]

Nirmatrelvir has significant drug-drug interactions due to the ritonavir component. As a potent CYP3A inhibitor, ritonavir can increase plasma concentrations of concomitant medications, increasing the risks of developing severe and life-threatening drug-related adverse effects. Due to these drug-drug interactions, many CYP3A-metabolized drugs are contraindicated in patients taking nirmatrelvir.[1]

In patients with undiagnosed or uncontrolled HIV-1 infection, there is a theoretical risk that the use of nirmatrelvir will facilitate the development of antiviral cross-resistance against HIV-1 protease inhibitors due to the ritonavir component, which is an HIV-1 protease inhibitor; hence nirmatrelvir use is cautioned in patients with undiagnosed or uncontrolled HIV-1 infection.[20]

Table 4: Adverse Reactions and Frequency Categories of Nirmatrelvir.

System organ class	Frequency category	Adverse reactions
Immune system disorders	Uncommon	Hypersensitivity including pruritus and rash
	Rare	Anaphylaxis
Nervous system disorders	Common	Dysgeusia, headache
Vascular disorders	Uncommon	Hypertension
Gastrointestinal disorders	Common	Diarrhoea, vomiting, nausea
	Uncommon	Abdominal pain
General disorders and administration site conditions	Rare	Malaise

Table 4. Adverse Reactions and Frequency Categories of Nirmatrelvir (table 4) It systematically details common, uncommon, and rare side effects, categorized by the affected body system. This data is crucial for clinicians and researchers to understand the potential risks associated with nirmatrelvir, aiding in informed decision-making and patient counselling.

Treatment for overdose

There is no specific antidote for overdose.[4]

Contraindication

Nirmatrelvir is contraindicated if the patient has a history of clinically significant hypersensitivity reactions (e.g., anaphylaxis, Stevens-Johnson syndrome, toxic epidermal necrolysis) to nirmatrelvir or ritonavir, other drugs in the same class, or drug components.

Moreover, nirmatrelvir is contraindicated with the concomitant use of medications that depend on CYP3A for clearance and whose elevated plasma concentrations are associated with serious and life-threatening adverse reactions which are due to the CYP3A-inhibiting effects of ritonavir, which can increase plasma concentrations of those medications to dangerous levels.

Furthermore, nirmatrelvir is contraindicated with the concomitant use of medications that are CYP3A inducers, which can decrease nirmatrelvir plasma concentrations to levels that result in loss of virologic response and development of antiviral resistance. This is due to nirmatrelvir being a CYP3A substrate whose plasma concentration is decreased by CYP3A inducers.[9]

Sublicensed companies

Fig. 6: Global Licensing of Nirmatrelvir Under Medicines Patent Pool.

Fig.6 Global Licensing of Nirmatrelvir Under Medicines Patent Pool (fig.6) This figure shows the companies sublicensed under the Medicines Patent Pool agreement to manufacture and distribute nirmatrelvir in 95 low- and middle-income countries, enabling broader global access.

Licensing

In November 2021, Pfizer signed a license agreement with the United Nations–backed Medicines Patent Pool to allow nirmatrelvir to be manufactured and sold in 95 countries. Pfizer stated that the agreement will allow local medicine manufacturers to produce the pill "with the goal of facilitating greater access to the global population". The deal excludes several countries with major COVID-19 outbreaks including Brazil, China, Russia, Argentina, and Thailand.[21]

RESEARCH

The research that led to nirmatrelvir began in March 2020, when Pfizer formally launched a project at its Cambridge, Massachusetts site to develop antiviral drugs for treating COVID-19. In July 2020, Pfizer chemists were able to synthesize nirmatrelvir for the first time. In September 2020, Pfizer completed a pharmacokinetic study in rats which suggested that nirmatrelvir could be administered orally. The actual synthesis of the drug for laboratory research and for clinical trials was carried out at Pfizer's Groton, Connecticut site. In February 2021, Pfizer launched the company's first phase I trial of PF-07321332 (nirmatrelvir) at its clinical research unit in New Haven, Connecticut. A study published in March 2023, finds that treatment with nirmatrelvir within five days of initial infection is shown to reduce risk of long COVID.[7]

CONCLUSION

This cohort study demonstrated that among individuals with SARS-CoV-2 infection and at least one risk factor for severe disease, early initiation of nirmatrelvir therapy (within five days of a positive test) was linked to a lower risk of developing post–COVID-19 condition (PCC). This association was observed across varying risk profiles, irrespective of vaccination status or prior infection history. These results indicate that the therapeutic benefits of nirmatrelvir may extend beyond the acute phase, potentially reducing long-term complications of COVID-19.

REFERENCE

1. Cruciani M, Pati I, Masiello F, Pupella S, De Angelis V. Nirmatrelvir/ritonavir for COVID-19: an overview of systematic reviews. J Antimicrob Chemother [Internet], 2024; 79(3): 477–97. Available from: https://doi.org/10.1093/jac/dkad376
2. Hashemian SMR, Sheida A, Taghizadieh M, Memar MY, Hamblin MR, Bannazadeh Baghi H, et al. Paxlovid (Nirmatrelvir/Ritonavir): A new approach to Covid-19 therapy?

Biomedicine and Pharmacotherapy, 2023.

3. Hung YP, Lee JC, Chiu CW, Lee CC, Tsai PJ, Hsu IL, et al. Oral Nirmatrelvir/Ritonavir Therapy for COVID-19: The Dawn in the Dark? Antibiotics, 2022.
4. Gerhart J, Cox DS, Singh RSP, Chan PLS, Rao R, Allen R, et al. A Comprehensive Review of the Clinical Pharmacokinetics, Pharmacodynamics, and Drug Interactions of Nirmatrelvir/Ritonavir. Clin Pharmacokinet [Internet], 2024; 63(1): 27–42. Available from: https://doi.org/10.1007/s40262-023-01339-y
5. Iketani S, Mohri H, Culbertson B, Hong SJ, Duan Y, Luck MI, et al. Multiple pathways for SARS-CoV-2 resistance to nirmatrelvir. Nature, 2023.
6. Wang Y, Zhao D, Chen X, Liu X, Xiao W, Feng L. The effect of nirmatrelvir-ritonavir on viral clearance and length of hospital stay in patients infected with SARS-CoV-2 omicron variants. Influenza Other Respi Viruses, 2023.
7. Hammond J, Leister-Tebbe H, Gardner A, Abreu P, Bao W, Wisemandle W, et al. Oral Nirmatrelvir for High-Risk, Nonhospitalized Adults with Covid-19. N Engl J Med., 2022.
8. Wong CKH, Mak LY, Au ICH, Cheng WY, So CH, Lau KTK, et al. Risk of acute liver injury following the nirmatrelvir/ritonavir use. Liver Int, 2023.
9. Chen W, Liang B, Wu X, Li L, Wang C, Xing D. Advances and challenges in using nirmatrelvir and its derivatives against SARS-CoV-2 infection. Journal of Pharmaceutical Analysis. 2023.
10. Xie Y, Choi T, Al-Aly Z. Association of Treatment With Nirmatrelvir and the Risk of Post-COVID-19 Condition. JAMA Intern Med. 2023.
11. Joyce RP, Hu VW, Wang J. The history, mechanism, and perspectives of nirmatrelvir (PF-07321332): an orally bioavailable main protease inhibitor used in combination with ritonavir to reduce COVID-19-related hospitalizations. Medicinal Chemistry Research. 2022.
12. Lamb YN. Nirmatrelvir Plus Ritonavir: First Approval. Drugs. 2022.
13. 13. Li J, Wang Y, Solanki K, Atre R, Lavrijsen M, Pan Q, et al. Nirmatrelvir exerts distinct antiviral potency against different human coronaviruses. Antiviral Res., 2023.
14. Carlin AF, Clark AE, Chaillon A, Garretson AF, Bray W, Porrachia M, et al. Virologic and Immunologic Characterization of Coronavirus Disease 2019 Recrudescence After Nirmatrelvir/Ritonavir Treatment. Clin Infect Dis., 2023.
15. Gentile I, Scotto R, Schiano Moriello N, Pinchera B, Villari R, Trucillo E, et al. Nirmatrelvir/Ritonavir and Molnupiravir in the Treatment of Mild/Moderate COVID-19: Results of a Real-Life Study. Vaccines, 2022.

16. Salmanton-García J, Marchesi F, Gomes da Silva M, Farina F, Dávila-Valls J, Bilgin YM, et al. Nirmatrelvir/ritonavir in COVID-19 patients with haematological malignancies: a report from the EPICOVIDEHA registry. eClinical Medicine., 2023.
17. Wan EYF, Yan VKC, Wong ZCT, Chui CSL, Lai FTT, Li X, et al. Effectiveness of molnupiravir vs nirmatrelvir-ritonavir in non-hospitalised and hospitalised patients with COVID-19: a target trial emulation study. eClinical Medicine, 2023.
18. Young C, Papiro T, Greenberg JH. Elevated tacrolimus levels after treatment with nirmatrelvir/ritonavir (Paxlovid) for COVID-19 infection in a child with a kidney transplant. Pediatr Nephrol, 2023.
19. Meskini M, Rezghi Rami M, Maroofi P, Ghosh S, Siadat SD, Sheikhpour M. An Overview on the Epidemiology and Immunology of COVID-19. Journal of Infection and Public Health, 2021.
20. Hu Y, Lewandowski EM, Tan H, Zhang X, Morgan RT, Zhang X, et al. Naturally Occurring Mutations of SARS-CoV-2 Main Protease Confer Drug Resistance to Nirmatrelvir. ACS Cent Sci., 2023.
21. Xie Y, Choi T, Al-Aly Z. Association of Treatment With Nirmatrelvir and the Risk of Post-COVID-19 Condition. JAMA Intern Med., 2023; 183(6): 554–64.