LOCAL PRODUCT DOCUMENT
PT. PFIZER INDONESIA

Generic Name: Nirmatrelvir/Ritonavir
Trade Name: PAXLOVID
CDS Effective Date: September 10, 2025
Supersedes: August 11, 2025

1. NAME OF THE MEDICINAL PRODUCT

PAXLOVID

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each pink nirmatrelvir film-coated tablet contains 150 mg of nirmatrelvir.

Each white ritonavir film-coated tablet contains 100 mg of ritonavir.

3. PHARMACEUTICAL FORM

Nirmatrelvir

Film-coated tablet.

Pink, oval, with a dimension of approximately 17.6 mm in length and 8.6 mm in width debossed with ‘PFE’ on one side and ‘3CL’ on the other side.

Ritonavir

Film-coated tablet.
White to off white, capsule shaped tablets, debossed with 'H' on one side and 'R9' on other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

PAXLOVID is indicated for the treatment of non-severe COVID-19 in adults who do not require supplemental oxygen and who are at increased risk for progression to severe COVID-19.

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4.2 Posology and method of administration

PAXLOVID is nirmatrelvir tablets co-packaged with ritonavir tablets.

Nirmatrelvir must be co-administered with ritonavir. Failure to correctly co-administer nirmatrelvir with ritonavir may result in plasma levels of nirmatrelvir that are insufficient to achieve the desired therapeutic effect.

Posology

The recommended dosage in adult is 300 mg nirmatrelvir (two 150 mg tablets) with 100 mg ritonavir (one 100 mg tablet) all taken together orally twice daily for 5 days. PAXLOVID should be given as soon as possible after a diagnosis of COVID-19 has been made and within 5 days of symptom onset even if baseline COVID-19 symptoms are mild. Completion of the full 5-day treatment course is recommended even if the patient requires hospitalization due to severe or critical COVID-19 after starting treatment with PAXLOVID.

If the patient misses a dose of PAXLOVID within 8 hours of the time it is usually taken, the patient should take it as soon as possible and resume the normal dosing schedule. If the patient misses a dose by more than 8 hours, the patient should not take the missed dose and instead take the next dose at the regularly scheduled time. The patient should not double the dose to make up for a missed dose.

Patient selection

The following medical conditions or other factors place adult at high risk for progression to severe COVID-19:

- Older age (e.g., 60 years of age and older)
- Obesity or being overweight [e.g., body mass index (BMI) >25 kg/m^2]
- Current smoker
- Chronic kidney disease
- Diabetes
- Immunosuppressive disease or prolonged use of immune weakening medications
- Cardiovascular disease (including congenital heart disease) or hypertension
- Chronic lung disease [e.g., chronic obstructive pulmonary disease, asthma (moderate to severe), interstitial lung disease, cystic fibrosis, and pulmonary hypertension]
- Sickle cell disease
- Neurodevelopmental disorders (e.g., cerebral palsy, Down's syndrome) or other conditions that confer medical complexity (e.g., genetic or metabolic syndromes and severe congenital anomalies)
- Active cancer

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- Medical-related technological dependence (e.g., CPAP [not related to COVID-19])

Other medical conditions or factors (e.g., race or ethnicity) may also place individual patients at high risk for progression to severe COVID-19 and the approved use of PAXLOVID is not limited to the medical conditions or factors listed above. Healthcare providers should consider the benefit-risk for an individual patient.

Special populations

Pediatric population
The safety and efficacy of PAXLOVID have not been studied in patients younger than 18 years of age.

Elderly
No dose adjustment is currently recommended for elderly patients.

Renal impairment
No dosage adjustment is needed in patients with mild renal impairment (eGFR ≥ 60 to <90 mL/min).

In patients with moderate renal impairment (eGFR ≥ 30 to <60 mL/min), the dose of PAXLOVID should be reduced to nirmatrelvir/ritonavir 150 mg/100 mg (1 tablet of each) twice daily for 5 days.

PAXLOVID is not recommended in patients with severe renal impairment (eGFR <30 mL/min) until more data are available; the appropriate dosage for patients with severe renal impairment has not been determined (see section 5.2).

Special attention for patients with moderate renal impairment

Healthcare providers should pay special attention to dosing instructions for patients with moderate renal impairment and alert the patient that the daily dose pack provided may contain more nirmatrelvir and ritonavir tablets than needed for accurate dosing in these patients.

Therefore, patients with moderate renal impairment should be alerted that only one tablet of nirmatrelvir with one tablet of ritonavir should be taken every 12 hours for 5 days.

Hepatic impairment
No dosage adjustment is needed in patients with mild (Child-Pugh Class A) or moderate (Child-Pugh Class B) hepatic impairment.

No pharmacokinetic or safety data are available regarding the use of nirmatrelvir or ritonavir in participants with severe (Child-Pugh Class C) hepatic impairment; therefore, PAXLOVID is not recommended for use in patients with severe hepatic impairment (see section 5.2).

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Concomitant therapy with ritonavir- or cobicistat-containing regimen
No dose adjustment is needed; the dose of PAXLOVID is 300 mg/100 mg twice daily for 5 days.

Patients diagnosed with human immunodeficiency virus (HIV) or hepatitis C virus (HCV) infection who are receiving ritonavir- or cobicistat-containing regimen should continue their treatment as indicated.

Method of administration

For oral use.

PAXLOVID can be taken with or without food (see section 5.2). The tablets should be swallowed whole and not chewed, broken, or crushed.

4.3 Contraindications

PAXLOVID is contraindicated in patients with a history of clinically significant hypersensitivity to the active substances (nirmatrelvir/ritonavir) or to any of the product excipients.

PAXLOVID is contraindicated with drugs that are highly dependent on CYP3A for clearance and for which elevated concentrations are associated with serious and/or life-threatening reactions (see section 4.5). Drugs listed in this section and section 4.5 are a guide and not considered a comprehensive list of all possible drugs that may be contraindicated with PAXLOVID.

- Alpha 1-adrenoreceptor antagonist: alfuzosin
- Analgesics: pethidine, piroxicam, propoxyphene
- Anticancer: neratinib, venetoclax
- Antianginal: ranolazine
- Antiarrhythmic: amiodarone, bepridil, dronedarone, encainide, flecainide, propafenone, quinidine
- Antibiotic: fusidic acid
- Anti-gout: colchicine
- Antihistamines: astemizole, terfenadine
- Antipsychotics: lurasidone, pimozide, clozapine, quetiapine
- Benign prostatic hyperplasia agents: silodosin
- Cardiovascular agents: eplerenone, ivabradine
- Ergot derivatives: dihydroergotamine, ergonovine, ergotamine, methylergonovine
- GI motility agent: cisapride
- HMG-CoA reductase inhibitors: lovastatin, simvastatin
- Immunosuppressants: voclosporin

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- Microsomal triglyceride transfer protein inhibitor: lomitapide
- Migraine medications: eletriptan, ubrogepant
- Mineralocorticoid receptor antagonists: finerenone
- Non-opioid analgesic (selective blocker of $Na_v1.8$ sodium channels): suzetrigine
- Opioid antagonists: naloxegol
- PDE5 inhibitor: avanafil, vardenafil, sildenafil (Revatio®) when used for pulmonary arterial hypertension (PAH)
- Sedative/hypnotics: clonazepam, diazepam, estazolam, flurazepam, triazolam, oral midazolam
- Serotonin receptor 1A agonist/serotonin receptor 2A antagonist: flibanserin
- Vasopressin receptor antagonists: tolvaptan

PAXLOVID is contraindicated with drugs that are potent CYP3A inducers where significantly reduced nirmatrelvir or ritonavir plasma concentrations may be associated with the potential for loss of virologic response and possible resistance. PAXLOVID cannot be started immediately after discontinuation of any of the following medications due to the delayed offset of the recently discontinued CYP3A inducer (see section 4.5).

- Anticancer drugs: apalutamide, enzalutamide
- Anticonvulsant: carbamazepine, phenobarbital, primidone, phenytoin
- Antimycobacterials: rifampin, rifapentine
- Cystic fibrosis transmembrane conductance regulator potentiators: lumacaftor/ivacaftor
- Herbal products: St. John's Wort (*Hypericum perforatum*)

4.4 Special warnings and precautions for use

Risk of serious adverse reactions due to drug interactions

Initiation of PAXLOVID, a CYP3A inhibitor, in patients receiving medications metabolized by CYP3A or initiation of medications metabolized by CYP3A in patients already receiving PAXLOVID, may increase plasma concentrations of medications metabolized by CYP3A.

Initiation of medications that inhibit or induce CYP3A may increase or decrease concentrations of PAXLOVID, respectively.

These interactions may lead to:

- Clinically significant adverse reactions, potentially leading to severe, life-threatening, or fatal events from greater exposures of concomitant medications.
- Clinically significant adverse reactions from greater exposures of PAXLOVID.

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- Loss of therapeutic effect of PAXLOVID and possible development of viral resistance.

Severe, life-threatening, and fatal adverse reactions due to drug interactions have been reported in patients treated with PAXLOVID.

See Table 1 for drugs that are contraindicated for concomitant use with nirmatrelvir/ritonavir and for potentially significant interactions with other drugs (see section 4.5; also see section 4.3 for drugs that are contraindicated for concomitant use). Potential for drug interactions should be considered prior to and during PAXLOVID therapy; concomitant medications should be reviewed during PAXLOVID therapy and the patient should be monitored for the adverse reactions associated with the concomitant medications.

Co-administration of PAXLOVID with calcineurin inhibitors and mTOR inhibitors
Consultation of a multidisciplinary group (e.g., involving physicians, specialists in immunosuppressive therapy, and/or specialists in clinical pharmacology) is required to handle the complexity of this co-administration by closely and regularly monitoring immunosuppressant blood concentrations and adjusting the dose of the immunosuppressant in accordance with the latest guidelines (see section 4.5).

Hypersensitivity reactions

Anaphylaxis, hypersensitivity reactions, and serious skin reactions (including toxic epidermal necrolysis and Stevens-Johnson syndrome) have been reported with PAXLOVID (see section 4.8). If signs and symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue PAXLOVID and initiate appropriate medications and/or supportive care.

Hepatotoxicity

Hepatic transaminase elevations, clinical hepatitis and jaundice have occurred in patients receiving ritonavir. Therefore, caution should be exercised when administering PAXLOVID to patients with pre-existing liver diseases, liver enzyme abnormalities, or hepatitis.

Risk of HIV-1 resistance development

Because nirmatrelvir is co-administered with ritonavir, there may be a risk of HIV-1 developing resistance to HIV protease inhibitors in individuals with uncontrolled or undiagnosed HIV-1 infection.

Excipients

Nirmatrelvir tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

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Nirmatrelvir and ritonavir tablets each contain less than 1 mmol sodium (23 mg) per dose, that is to say essentially ‘sodium-free’.

4.5 Interaction with other medicinal products and other forms of interaction

PAXLOVID (nirmatrelvir/ritonavir) is a strong inhibitor of CYP3A and an inhibitor of CYP2D6, P-gp and OATP1B1. Co-administration of PAXLOVID with drugs that are primarily metabolized by CYP3A and CYP2D6 or are transported by P-gp or OATP1B1 may result in increased plasma concentrations of such drugs and increase the risk of adverse reactions.

Drugs that are extensively metabolized by CYP3A and have high first pass metabolism appear to be the most susceptible to large increases in exposure when co-administered with nirmatrelvir/ritonavir. Thus, co-administration of PAXLOVID with drugs highly dependent on CYP3A for clearance and for which elevated plasma concentrations are associated with serious and/or life-threatening events is contraindicated (see section 4.3).

In vitro study results showed nirmatrelvir may be inducer of CYP3A4, CYP2B6, CYP2C8, and CYP2C9. The clinical relevance is unknown. Based on *in vitro* data, nirmatrelvir has a low potential to inhibit BCRP, MATE2K, OAT1, OAT3, OATP1B3 and OCT2. There is a potential for nirmatrelvir to inhibit MDR1, MATE1, OCT1 and OATP1B1 at clinically relevant concentrations.

Ritonavir has a high affinity for several cytochrome P450 (CYP) isoforms and may inhibit oxidation with the following ranked order: CYP3A4 > CYP2D6. Ritonavir also has a high affinity for P glycoprotein (P-gp) and may inhibit this transporter. Ritonavir may induce glucuronidation and oxidation by CYP1A2, CYP2C8, CYP2C9 and CYP2C19 thereby increasing the biotransformation of some medicinal products metabolised by these pathways and may result in decreased systemic exposure to such medicinal products, which could decrease or shorten their therapeutic effect.

Co-administration of other CYP3A4 substrates that may lead to potentially significant interaction should be considered only if the benefits outweigh the risks (see Table 1).

Nirmatrelvir and ritonavir are CYP3A substrates; therefore, drugs that induce CYP3A may decrease nirmatrelvir and ritonavir plasma concentrations and reduce PAXLOVID therapeutic effect.

Drugs listed in Table 1 are a guide and not considered a comprehensive list of all possible drugs that may interact with nirmatrelvir/ritonavir. The healthcare provider should consult appropriate references for comprehensive information.

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Table 1: Established and other potentially significant drug interactions			
Drug Class	**Drugs within Class**	**Effect on Concentration**	**Clinical Comments**
Alpha 1-adrenoreceptor antagonist	alfuzosin	↑ alfuzosin	Co-administration contraindicated due to potential hypotension (see section 4.3).
Alpha 1-adrenoreceptor antagonist	tamsulosin	↑ tamsulosin	Avoid concomitant use with PAXLOVID.
Amphetamine derivatives	methylphenidate, dexamfetamine	↑ methylphenidate, ↑ dexamfetamine	Ritonavir dosed as an antiretroviral agent is likely to inhibit CYP2D6 and as a result is expected to increase concentrations of amphetamine and its derivatives. Careful monitoring of adverse effects is recommended when these medicines are co-administered with PAXLOVID.
Analgesics	buprenorphine norbuprenorphine	↑ buprenorphine, ↑ norbuprenorphine	The increases of plasma levels of buprenorphine and its active metabolite did not lead to clinically significant pharmacodynamic changes in a population of opioid tolerant patients. Adjustment to the dose of buprenorphine may therefore not be necessary when the two are dosed together.
Antianginal	ranolazine	↑ ranolazine	Co-administration contraindicated due to potential for serious and/or life-threatening reactions (see section 4.3).
Antiarrhythmics	amiodarone, dronedarone, flecainide, propafenone, quinidine	↑ antiarrhythmic	Co-administration contraindicated due to potential for cardiac arrhythmias (see section 4.3).
Antiarrhythmics	lidocaine (systemic), disopyramide	↑ antiarrhythmic	Caution is warranted and therapeutic concentration monitoring is recommended for antiarrhythmics if available.
Antiasthmatic	theophylline	↓ theophylline	An increased dose of theophylline may be required when coadministered with ritonavir, due to induction of CYP1A2.
Anticancer drugs	apalutamide, enzalutamide	↓ nirmatrelvir/ritonavir	Co-administration contraindicated due to potential loss of virologic response and possible resistance (see section 4.3).

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Table 1: Established and other potentially significant drug interactions

Drug Class	Drugs within Class	Effect on Concentration	Clinical Comments
Anticancer drugs	abemaciclib, ceritinib, dasatinib, encorafenib, ibrutinib, ivosidenib, neratinib, nilotinib, venetoclax vinblastine, vincristine	↑ anticancer drug	Avoid co-administration of encorafenib or ivosidenib due to potential risk of serious adverse events such as QT interval prolongation. Use of neratinib and venetoclax is contraindicated. Avoid use of ibrutinib. Co-administration of vincristine and vinblastine may lead to significant hematologic or gastrointestinal side effects.
	afatinib		Serum concentrations may be increased due to Breast Cancer Resistance Protein (BCRP) and acute P-gp inhibition by ritonavir. The extent of increase in AUC and C_{max} depends on the timing of ritonavir administration. Caution should be exercised in administering afatinib with PAXLOVID. Monitor for ADRs related to afatinib.
	fostamatinib		Coadministration of fostamatinib with ritonavir may increase fostamatinib metabolite R406 exposure resulting in dose-related adverse events such as hepatotoxicity, neutropenia, hypertension or diarrhoea. For further information, refer to the individual product label for anticancer drug.
Anticoagulants	warfarin	↑↓ warfarin	Closely monitor INR if co-administration with warfarin is necessary.
	rivaroxaban	↑ rivaroxaban	Increased bleeding risk with rivaroxaban. Avoid concomitant use.
	dabigatran[a]	↑ dabigatran	Increased bleeding risk with dabigatran. Depending on dabigatran indication and renal function, reduce dose of dabigatran or avoid concomitant use. Refer to

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Table 1: Established and other potentially significant drug interactions			
Drug Class	**Drugs within Class**	**Effect on Concentration**	**Clinical Comments**
			the dabigatran product label for further information.
	apixaban	↑ apixaban	Combined P-gp and strong CYP3A4 inhibitors increase blood levels of apixaban and increase the risk of bleeding. Dosing recommendations for co-administration of apixaban with PAXLOVID depend on the apixaban dose. Refer to the apixaban product label for more information.
Anticonvulsants	carbamazepine[a], phenobarbital, phenytoin, primidone	↓ nirmatrelvir/ritonavir	Co-administration contraindicated due to potential loss of virologic response and possible resistance (see section 4.3).
Antidepressants	bupropion	↓ bupropion and active metabolite hydroxy-bupropion	Monitor for an adequate clinical response to bupropion.
	trazodone	↑ trazodone	Adverse reactions of nausea, dizziness, hypotension, and syncope have been observed following co-administration of trazodone and ritonavir. A lower dose of trazodone should be considered. Refer to the trazadone product label for further information.

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Table 1: Established and other potentially significant drug interactions			
Drug Class	**Drugs within Class**	**Effect on Concentration**	**Clinical Comments**
Antidepressants	amitriptyline, fluoxetine, imipramine, nortriptyline, paroxetine, sertraline	↑ amitriptyline, ↑ fluoxetine, ↑ imipramine, ↑ nortriptyline, ↑ paroxetine, ↑ sertraline	Ritonavir dosed as an antiretroviral agent is likely to inhibit CYP2D6 and as a result is expected to increase concentrations of imipramine, amitriptyline, nortriptyline, fluoxetine, paroxetine or sertraline. Careful monitoring of therapeutic and adverse effects is recommended when these medicines are concomitantly administered with antiretroviral doses of ritonavir.
	desipramine	↑ desipramine	The AUC and C_{max} of the 2-hydroxy metabolite were decreased 15% and 67%, respectively. Dosage reduction of desipramine is recommended when coadministered with ritonavir.
Antifungals	voriconazole	↓ voriconazole	Avoid concomitant use of voriconazole.
	ketoconazole, isavuconazonium sulfate, itraconazole[a]	↑ ketoconazole ↑ isavuconazonium sulfate ↑ itraconazole	Refer to the ketoconazole, isavuconazonium sulfate, and itraconazole product labels for further information.
	nirmatrelvir/ ritonavir	↑ nirmatrelvir/ritonavir	A nirmatrelvir/ritonavir dose reduction is not needed.
Anti-gout	colchicine	↑ colchicine	Co-administration contraindicated due to potential for serious and/or life-threatening reactions in patients with renal and/or hepatic impairment (see section 4.3).
Anti-HIV protease inhibitors	atazanavir, darunavir, tipranavir, amprenavir, fosamprenavir	↑ protease inhibitor	For further information, refer to the respective protease inhibitors' product labels. Patients on ritonavir- or cobicistat-containing HIV regimens should continue their treatment as indicated. Monitor for increased PAXLOVID or protease inhibitor adverse events (see section 4.2).

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Table 1: Established and other potentially significant drug interactions			
Drug Class	**Drugs within Class**	**Effect on Concentration**	**Clinical Comments**
Anti-HIV	efavirenz, maraviroc, nevirapine, zidovudine, bictegravir/ emtricitabine/ tenofovir, raltegravir	↑ efavirenz ↑ maraviroc ↑ nevirapine ↓ zidovudine ↑ bictegravir ↔ emtricitabine ↑ tenofovir ↓ raltegravir	For further information, refer to the respective anti-HIV drugs' product label.
Antihistamines	fexofenadine,	↑ fexofenadine	Ritonavir may modify P-gp mediated fexofenadine efflux when dosed as a pharmacokinetic enhancer resulting in increased concentrations of fexofenadine.
	loratadine	↑ loratadine	Ritonavir dosed as a pharmacokinetic enhancer inhibits CYP3A and as a result is expected to increase the plasma concentrations of loratadine. Careful monitoring of therapeutic and adverse effects is recommended when loratadine is coadministered with ritonavir.
	terfenadine	↑ terfenadine	Increased plasma concentrations of terfenadine. Thereby, increasing the risk of serious arrhythmias from this agent and therefore concomitant use with PAXLOVID is contraindicated (see section 4.3).
Anti-infective	clarithromycin, erythromycin	↑ clarithromycin ↑ erythromycin	Refer to the respective product label for anti-infective dose adjustment.
	atovaquone	↓ atovaquone	Ritonavir dosed as a pharmacokinetic enhancer induces glucuronidation and as a result is expected to decrease the plasma concentrations of atovaquone. Careful monitoring of serum levels or therapeutic effects is recommended when atovaquone is coadministered with ritonavir.
	delamanid		No interaction study is available with ritonavir only. In a healthy volunteer drug interaction study of delamanid 100 mg twice daily and lopinavir/ritonavir 400/100 mg

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Table 1: Established and other potentially significant drug interactions			
Drug Class	**Drugs within Class**	**Effect on Concentration**	**Clinical Comments**
			twice daily for 14 days, the exposure of the delamanid metabolite DM 6705 was 30% increased. Due to the risk of QTc prolongation associated with DM-6705, if coadministration of delamanid with ritonavir is considered necessary, very frequent ECG monitoring throughout the full delamanid treatment period is recommended.
	sulfamethoxazole/ trimethoprim		Dose alteration of sulfamethoxazole/trimethoprim during concomitant ritonavir therapy should not be necessary.
Antimycobacterial	rifampin, rifapentine	↓ nirmatrelvir/ritonavir	Co-administration contraindicated due to potential loss of virologic response and possible resistance. Alternate antimycobacterial drugs such as rifabutin should be considered (see section 4.3).
Antimycobacterial	bedaquiline	↑ bedaquiline	Refer to the bedaquiline product label for further information.
	rifabutin	↑ rifabutin	Refer to the rifabutin product label for further information on rifabutin dose reduction.
Antiparasitic agent	albendazole	↓ albendazole	Significant decreases in plasma concentrations of albendazole and its active metabolite may occur due to induction by ritonavir, with a risk of decreased albendazole efficacy. Clinical monitoring of therapeutic response and possible adjustment of albendazole dosage during treatment with PAXLOVID and following discontinuation is recommended.
Antipsychotics	lurasidone, pimozide	↑ lurasidone ↑ pimozide	Co-administration contraindicated due to serious and/or life-threatening reactions such as cardiac arrhythmias (see section 4.3).

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Table 1: Established and other potentially significant drug interactions			
Drug Class	**Drugs within Class**	**Effect on Concentration**	**Clinical Comments**
Antipsychotics	quetiapine	↑ quetiapine	Due to CYP3A inhibition by ritonavir, concentrations of quetiapine are expected to increase. Concomitant administration of PAXLOVID and quetiapine is contraindicated as it may increase quetiapine-related toxicity (see section 4.3)
	clozapine	↑ clozapine	Ritonavir coadministration is likely to result in increased plasma concentrations of clozapine and is therefore contraindicated (see section 4.3)
Benign prostatic hyperplasia agents	silodosin	↑ silodosin	Co-administration contraindicated due to potential for postural hypotension (see section 4.3).
Calcium channel blockers	amlodipine, diltiazem, felodipine, nicardipine, nifedipine, verapamil	↑ calcium channel blocker	Caution is warranted and clinical monitoring of patients is recommended. A dose decrease may be needed for these drugs when co-administered with PAXLOVID. If co-administered, refer to the individual product label for calcium channel blocker for further information.
Cardiac glycosides	digoxin	↑ digoxin	Caution should be exercised when co-administering PAXLOVID with digoxin, with appropriate monitoring of serum digoxin levels. Refer to the digoxin product label for further information.
Cardiovascular agents	eplerenone	↑ eplerenone	Co-administration with eplerenone is contraindicated due to potential for hyperkalemia (see section 4.3).
	ivabradine	↑ ivabradine	Co-administration with ivabradine is contraindicated due to potential for bradycardia or conduction disturbances (see section 4.3).

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Table 1: Established and other potentially significant drug interactions

Drug Class	Drugs within Class	Effect on Concentration	Clinical Comments
Cardiovascular agents	aliskiren, ticagrelor, vorapaxar	↑ aliskiren ↑ ticagrelor ↑ vorapaxar	Avoid concomitant use with PAXLOVID.
	clopidogrel	↓ clopidogrel active metabolite	
	cilostazol	↑ cilostazol	Dosage adjustment of cilostazol is recommended. Refer to the cilostazol product label for more information.
	mavacamten	↑ mavacamten	Co-administration with mavacamten may increase mavacamten plasma concentration and increase the risk of heart failure. Discontinue mavacamten for the duration of PAXLOVID treatment. Resumption of mavacamten within 5 days of completing PAXLOVID may result in higher exposure of mavacamten. Refer to the mavacamten product label for more information.
Corticosteroids primarily metabolized by CYP3A	betamethasone, budesonide, ciclesonide, dexamethasone, fluticasone, methylprednisolone, mometasone, triamcinolone	↑ corticosteroid	Co-administration with corticosteroids (all routes of administration) of which exposures are significantly increased by strong CYP3A inhibitors can increase the risk for Cushing's syndrome and adrenal suppression. However, the risk of Cushing's syndrome and adrenal suppression associated with short-term use of a strong CYP3A4 inhibitor is low. Alternative corticosteroids including beclomethasone, prednisone, and prednisolone should be considered.
Cystic fibrosis transmembrane conductance regulator potentiators	lumacaftor/ivacaftor	↓ nirmatrelvir/ritonavir	Co-administration contraindicated due to potential loss of virologic response and possible resistance (see section 4.3).

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Table 1: Established and other potentially significant drug interactions			
Drug Class	**Drugs within Class**	**Effect on Concentration**	**Clinical Comments**
Cystic fibrosis transmembrane conductance regulator potentiators	ivacaftor elexacaftor/ tezacaftor/ivacaftor tezacaftor/ivacaftor	↑ ivacaftor ↑ elexacaftor/ tezacaftor/ivacaftor ↑ tezacaftor/ivacaftor	Reduce dosage when co-administered with PAXLOVID. Refer to the individual product labels for more information.
Dipeptidyl peptidase 4 (DPP4) inhibitors	saxagliptin	↑ saxagliptin	Dosage adjustment of saxagliptin is recommended. Refer to the saxagliptin product label for more information.
Endothelin receptor antagonists	bosentan riociguat	↑ bosentan ↑ riociguat	Discontinue use of bosentan at least 36 hours prior to initiation of PAXLOVID. Refer to the bosentan product label for further information. Serum concentrations may be increased due to CYP3A and P-gp inhibition by ritonavir. The coadministration of riociguat with PAXLOVID is not recommended (refer to riociguat product label).
Ergot derivatives	dihydroergotamine, ergonovine, ergotamine, methylergonovine	↑ dihydroergotamine ↑ ergonovine ↑ ergotamine ↑ methylergonovine	Co-administration contraindicated due to potential for acute ergot toxicity characterized by vasospasm and ischemia of the extremities and other tissues including the central nervous system (see section 4.3).
Hepatitis C direct acting antivirals	elbasvir/grazoprevir, glecaprevir/pibrentasvir ombitasvir/paritaprevir/ ritonavir and dasabuvir sofosbuvir/velpatasvir/ voxilaprevir	↑ antiviral	Increased grazoprevir concentrations can result in ALT elevations. Avoid concomitant use of glecaprevir/pibrentasvir with PAXLOVID. Refer to the ombitasvir/paritaprevir/ritonavir and dasabuvir label for further information. Refer to the sofosbuvir/velpatasvir/voxilaprevir product label for further information.

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Table 1: Established and other potentially significant drug interactions			
Drug Class	**Drugs within Class**	**Effect on Concentration**	**Clinical Comments**
			Patients on ritonavir-containing HCV regimens should continue their treatment as indicated. Monitor for increased PAXLOVID or HCV drug adverse events with concomitant use (see section 4.2).
Herbal products	St. John's Wort (*Hypericum perforatum*)	↓ nirmatrelvir/ritonavir	Co-administration contraindicated due to potential loss of virologic response and possible resistance (see section 4.3).
HMG-CoA reductase inhibitors	lovastatin, simvastatin	↑ lovastatin ↑ simvastatin	Co-administration contraindicated due to potential for myopathy including rhabdomyolysis (see section 4.3). Discontinue use of lovastatin and simvastatin at least 12 hours prior to initiation of PAXLOVID, during the 5 days of PAXLOVID treatment and for 5 days after completing PAXLOVID.
HMG-CoA reductase inhibitors	atorvastatin, rosuvastatin[a]	↑ atorvastatin ↑ rosuvastatin	Consider temporary discontinuation of atorvastatin and rosuvastatin during treatment with PAXLOVID. Atorvastatin and rosuvastatin do not need to be held prior to or after completing PAXLOVID.
	fluvastatin, pravastatin	↑ fluvastatin, ↑ pravastatin	The metabolism of pravastatin and fluvastatin is not dependent on CYP3A, and interactions are not expected with ritonavir. If treatment with an HMG-CoA reductase inhibitor is indicated, pravastatin or fluvastatin is recommended.
Hormonal contraceptive	ethinyl estradiol	↓ ethinyl estradiol	An additional, non-hormonal method of contraception should be considered during the 5 days of PAXLOVID treatment and until one menstrual cycle after stopping PAXLOVID.
Immunosuppressants	voclosporin	↑ voclosporin	Co-administration contraindicated due to potential for acute and/or chronic nephrotoxicity (see section 4.3).

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Table 1: Established and other potentially significant drug interactions

Drug Class	Drugs within Class	Effect on Concentration	Clinical Comments
Immunosuppressants	Calcineurin inhibitors: cyclosporine, tacrolimus mTOR inhibitors: everolimus, sirolimus	↑ cyclosporine ↑ tacrolimus ↑ everolimus ↑ sirolimus	Avoid concomitant use of calcineurin inhibitors and mTOR inhibitors during treatment with PAXLOVID. Dose adjustment of the immunosuppressant and close and regular monitoring for immunosuppressant concentrations and immunosuppressant-associated adverse reactions are recommended during and after treatment with PAXLOVID. Refer to the individual immunosuppressant product label and latest guidelines for further information and obtain expert consultation of a multidisciplinary group (see section 4.4).
Janus kinase (JAK) inhibitors	tofacitinib upadacitinib	↑ tofacitinib ↑ upadacitinib	Dosage adjustment of tofacitinib is recommended. Refer to the tofacitinib product label for more information. Dosing recommendations for co-administration of upadacitinib with PAXLOVID depends on the upadacitinib indication. Refer to the upadacitinib product label for more information.
Long-acting beta-adrenoceptor agonist	salmeterol	↑ salmeterol	Avoid concomitant use with PAXLOVID. The combination may result in increased risk of cardiovascular adverse events associated with salmeterol, including QT prolongation, palpitations, and sinus tachycardia.
Microsomal triglyceride transfer protein (MTTP) inhibitor	lomitapide	↑ lomitapide	Co-administration contraindicated due to potential for hepatotoxicity and gastrointestinal adverse reactions (see section 4.3).

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Table 1: Established and other potentially significant drug interactions			
Drug Class	**Drugs within Class**	**Effect on Concentration**	**Clinical Comments**
Migraine medications	eletriptan	↑ eletriptan	Co-administration of eletriptan within at least 72 hours of PAXLOVID is contraindicated due to potential for serious adverse reactions including cardiovascular and cerebrovascular events (see section 4.3).
	ubrogepant	↑ ubrogepant	Co-administration of ubrogepant with PAXLOVID is contraindicated due to potential for serious adverse reactions (see section 4.3).
Migraine medications	rimegepant	↑ rimegepant	Avoid concomitant use with PAXLOVID.
Mineralocorticoid receptor antagonists	finerenone	↑ finerenone	Co-administration contraindicated due to potential for serious adverse reactions including hyperkalemia, hypotension, and hyponatremia (see section 4.3).
Muscarinic receptor antagonists	darifenacin	↑ darifenacin	The darifenacin daily dose should not exceed 7.5 mg when co-administered with PAXLOVID. Refer to the darifenacin product label for more information.
Narcotic analgesics	fentanyl, hydrocodone, oxycodone, meperidine	↑ fentanyl ↑ hydrocodone ↑ oxycodone ↑ meperidine	Careful monitoring of therapeutic and adverse effects (including potentially fatal respiratory depression) is recommended when fentanyl, hydrocodone, oxycodone, or meperidine is concomitantly administered with PAXLOVID. If concomitant use with PAXLOVID is necessary, consider a dosage reduction of the narcotic analgesic and monitor patients closely at frequent intervals. Refer to the individual product label for more information.
	methadone	↓ methadone	Monitor methadone-maintained patients closely for evidence of withdrawal effects and adjust the methadone dose accordingly.
	morphine	↓ morphine	Morphine levels may be decreased due to induction of glucuronidation

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Table 1: Established and other potentially significant drug interactions			
Drug Class	**Drugs within Class**	**Effect on Concentration**	**Clinical Comments**
			by coadministered ritonavir dosed as a pharmacokinetic enhancer.
Neuropsychiatric agents	suvorexant	↑ suvorexant	Avoid concomitant use of suvorexant with PAXLOVID.
	aripiprazole, brexpiprazole, cariprazine, iloperidone, lumateperone, pimavanserin	↑ aripiprazole ↑ brexpiprazole ↑ cariprazine ↑ iloperidone ↑ lumateperone ↑ pimavanserin	Dosage adjustment of aripiprazole, brexpiprazole, cariprazine, iloperidone, lumateperone, and pimavanserin is recommended. Refer to the individual product label for more information.
Non-opioid analgesic (selective blocker of $Na_v1.8$ sodium channels)	suzetrigine	↑ suzetrigine and active metabolite M6-SUZ	Co-administration contraindicated due to potential for serious and/or life-threatening suzetrigine adverse reactions (see section 4.3).
Pulmonary hypertension agents (PDE5 inhibitors)	sildenafil (Revatio®)	↑ sildenafil	Co-administration of sildenafil with PAXLOVID is contraindicated due to the potential for sildenafil associated adverse events, including visual abnormalities, hypotension, prolonged erection, and syncope (see section 4.3).
Pulmonary hypertension agents (PDE5 inhibitors)	tadalafil (Adcirca®)	↑ tadalafil	Avoid concomitant use of tadalafil with PAXLOVID.
Pulmonary hypertension agents (sGC stimulators)	riociguat	↑ riociguat	Dosage adjustment is recommended for riociguat. Refer to the riociguat product label for more information.
Erectile dysfunction agents (PDE5 inhibitors)	avanafil, vardenafil	↑ avanafil ↑ vardenafil	Concomitant use of avanafil and vardenafil with PAXLOVID is contraindicated (see section 4.3)
	sildenafil, tadalafil	↑ sildenafil ↑ tadalafil	Dosage adjustment is recommended for use of sildenafil or tadalafil with PAXLOVID. Refer to the individual product label for more information.
Opioid antagonists	naloxegol	↑ naloxegol	Co-administration contraindicated due to the potential for opioid withdrawal symptoms (see section 4.3).
Sedative/hypnotics	triazolam, oral midazolam[a]	↑ triazolam ↑ midazolam	Co-administration contraindicated due to potential for extreme sedation and respiratory depression (see section 4.3).

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Table 1: Established and other potentially significant drug interactions

Drug Class	Drugs within Class	Effect on Concentration	Clinical Comments
Sedative/hypnotics	buspirone, zolpidem, alprazolam	↑ sedative/hypnotic	A dose decrease may be needed for these drugs when co-administered with PAXLOVID and monitoring for adverse events.
	clonazepam, diazepam, estazolam, flurazepam	↑clonazepam, ↑diazepam, ↑estazolam, ↑flurazepam	Ritonavir coadministration is likely to result in increased plasma concentrations of clonazepam, diazepam, estazolam and flurazepam and is therefore contraindicated (see section 4.3)
	midazolam (administered parenterally)	↑ midazolam	Co-administration of midazolam (parenteral) should be done in a setting which ensures close clinical monitoring and appropriate medical management in case of respiratory depression and/or prolonged sedation. Dosage reduction for midazolam should be considered, especially if more than a single dose of midazolam is administered. Refer to the midazolam product label for further information.
Serotonin receptor 1A agonist/ serotonin receptor 2A antagonist	flibanserin	↑ flibanserin	Co-administration contraindicated due to potential for hypotension, syncope, and CNS depression (see section 4.3).
Thyroid hormone replacement therapy	levothyroxine		Post-marketing cases have been reported indicating a potential interaction between ritonavir containing products and levothyroxine. Thyroid-stimulating hormone (TSH) should be monitored in patients treated with levothyroxine at least the first month after starting and/or ending ritonavir treatment.
Vasopressin receptor antagonists	tolvaptan	↑ tolvaptan	Co-administration contraindicated due to potential for dehydration, hypovolemia and hyperkalemia (see section 4.3).

a. See section 5.2 Drug interaction studies conducted with nirmatrelvir/ritonavir.

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4.6. Fertility, pregnancy and lactation

Women of childbearing potential/Contraception in males and females

There are limited human data on the use of PAXLOVID during pregnancy to inform the drug associated risk of adverse developmental outcomes; women of childbearing potential should avoid becoming pregnant during treatment with PAXLOVID and for 7 days after completing PAXLOVID treatment.

Use of ritonavir may reduce the efficacy of combined hormonal contraceptives. Patients using combined hormonal contraceptives should be advised to use an effective alternative contraceptive method or an additional barrier method of contraception during treatment with PAXLOVID, and until one menstrual cycle after stopping PAXLOVID (see section 4.5).

Pregnancy

There are limited data from the use of PAXLOVID in pregnant women. PAXLOVID is not recommended during pregnancy and in women of childbearing potential not using effective contraception.

There was no nirmatrelvir-related effect on fetal morphology or embryo-fetal viability at any dose tested in rat or rabbit embryo-fetal developmental toxicity studies (see section 5.3).

A large number of pregnant women were exposed to ritonavir during pregnancy. These data largely refer to exposures where ritonavir was used in combination therapy and not at therapeutic ritonavir doses but at lower doses as a pharmacokinetic enhancer for other protease inhibitors, similar to the ritonavir dose used for nirmatrelvir/ritonavir. These data indicate no increase in the rate of birth defects compared to rates observed in population-based birth defect surveillance systems.

Animal data with ritonavir have shown reproductive toxicity (see section 5.3).

Breast-feeding

In a clinical pharmacokinetics study, 8 healthy lactating women who were at least 12 weeks postpartum were administered 3 doses (steady-state dosing) of 300 mg/100 mg nirmatrelvir/ritonavir. Nirmatrelvir and ritonavir were excreted in breastmilk in small amounts, with a milk to plasma AUC ratio of 0.26 and 0.07, respectively. The estimated daily infant dose (assuming average milk consumption of 150 mL/kg/day), was 1.8% and 0.2% of the maternal dose.

There are no available data on the effects of nirmatrelvir or ritonavir on the breast fed newborn/infant or on milk production. A risk to the newborn/infant cannot be excluded. Breast feeding should be discontinued during treatment with PAXLOVID and for 48 hours after completing PAXLOVID treatment.

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Fertility

There are no human data on the effect of PAXLOVID on fertility. No human data on the effect of nirmatrelvir on fertility are available. Nirmatrelvir produced no effects on fertility in rats (see section 5.3).

There are no human data on the effect of ritonavir on fertility. Ritonavir produced no effects on fertility in rats.

4.7 Effects on ability to drive and use machines

There are no clinical studies that evaluated the effects of PAXLOVID on ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

The safety of PAXLOVID is based on data from phase 2/3 randomized, placebo-controlled trials in adult participants 18 years of age and older (see section 5.1).

- Study C4671005 (EPIC-HR) investigated PAXLOVID (nirmatrelvir/ritonavir 300 mg/100 mg) every 12 hours for 5 days in symptomatic participants with a laboratory confirmed diagnosis of SARS-CoV-2 infection. Participants were to present with mild-to-moderate COVID-19 at baseline.

Tabulated summary of adverse reactions

The adverse reactions in Table 2 are listed below by system organ class and frequency.

Table 2: Adverse Drug Reactions (ADRs) by System Organ Class and Council for International Organizations of Medical Sciences (CIOMS) Frequency Category Listed in Order of Decreasing Medical Seriousness or Clinical Importance Within Each Frequency Category and SOC

System Organ Class	Common ≥1/100 to <1/10	Uncommon ≥1/1,000 to <1/100	Rare ≥1/10,000 to <1/1,000
Immune system disorders		Hypersensitivity*	Anaphylaxis*
Nervous system disorders	Dysgeusia[a] Headache[a]		
Vascular disorders		Hypertension*	
Gastrointestinal disorders	Diarrhoea[a] Nausea*	Vomiting[a] Abdominal pain*	

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System Organ Class	Common ≥1/100 to <1/10	Uncommon ≥1/1,000 to <1/100	Rare ≥1/10,000 to <1/1,000
Skin and subcutaneous tissue disorders			Toxic epidermal necrolysis* Stevens-Johnson syndrome*
General disorders and administration site conditions			Malaise*
* Adverse drug reaction (ADR) identified post-marketing. a. Occurring at a ≥1% frequency in the PAXLOVID group and at a greater frequency than in the placebo group and/or likely associated with PAXLOVID based on available data and causality assessment.			

Paediatric population

The safety and efficacy of PAXLOVID in paediatric patients have not been established.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via:

Pusat Farmakovigilans/MESO Nasional
Direktorat Pengawasan Keamanan, Mutu, dan Ekspor Impor Obat, Narkotika, Psikotropika, Prekursor dan Zat Adiktif
Badan Pengawas Obat dan Makanan
Jl. Percetakan Negara No. 23, Jakarta Pusat, 10560
Email: pv-center@pom.go.id
Phone: +62-21-4244691 Ext.1079
Website: https://e-meso.pom.go.id/ADR

PT Pfizer Indonesia
Email: IDN.AEReporting@pfizer.com
Website: www.pfizersafetyreporting.com

4.9 Overdose

Treatment of overdose with PAXLOVID should consist of general supportive measures including monitoring of vital signs and observation of the clinical status of the patient. There is no specific antidote for overdose with PAXLOVID.

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5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Mechanism of action

Nirmatrelvir is a peptidomimetic inhibitor of the coronavirus 3C-like protease (3CL) including the SARS-CoV-2 3CL protease. Inhibition of the 3CL protease renders the protein incapable of processing polyprotein precursors which leads to the prevention of viral replication.

Nirmatrelvir was shown to be a potent inhibitor of SARS-CoV-2 3CL protease (Ki=0.00311 μM or IC50=0.0192 μM) in a biochemical enzymatic assay.

Ritonavir is not active against SARS-CoV-2 3CL protease. Ritonavir inhibits the CYP3A-mediated metabolism of nirmatrelvir, thereby providing increased plasma concentrations of nirmatrelvir.

Antiviral activity

In vitro antiviral activity
Nirmatrelvir exhibited antiviral activity against SARS-CoV-2 infection of differentiated normal human bronchial epithelial (dNHBE) cells, a primary human lung alveolar epithelial cell line (EC_{50} value of 61.8 nM and EC_{90} value of 181 nM) after 3 days of drug exposure.

The antiviral activity of nirmatrelvir against the Omicron sub-variants BA.2, BA.2.12.1, BA.4, BA.4.6, BA.5, BF.7 (P252L+F294L), BF.7 (T243I), BQ.1.11, BQ.1, XBB.1.5, EG.5, and JN.1 was assessed in Vero E6-TMPRSS2 cells in the presence of a P-gp inhibitor. Nirmatrelvir had a median EC_{50} value of 88 nM (range: 39-146 nM) against the Omicron sub-variants, reflecting EC_{50} value fold changes $\leq$ 1.8 relative to the USA-WA1/2020 isolate.

In addition, the antiviral activity of nirmatrelvir against the SARS-CoV-2 Alpha, Beta, Gamma, Delta, Lambda, Mu, and Omicron BA.1 variants was assessed in Vero E6 P-gp knockout cells. Nirmatrelvir had a median EC_{50} value of 25 nM (range: 16-141 nM). The Beta variant was the least susceptible variant tested, with an EC50 value fold-change of 3.7 relative to USA WA1/2020. The other variants had EC_{50} value fold-changes $\leq$ 1.1 relative to USA WA1/2020.

Antiviral activity against SARS-CoV-2 in animal models
Nirmatrelvir showed antiviral activity in BALB/c and 129 mice infected with mouse-adapted SARS-CoV-2. Oral administration of nirmatrelvir at 300 mg/kg or 1000 mg/kg twice daily initiated 4 hours post-inoculation or 1000 mg/kg twice daily initiated 12 hours post-inoculation resulted in reduction of lung viral titers and ameliorated indicators of disease (weight loss and lung pathology) compared to placebo-treated animals.

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Antiviral resistance in cell culture and biochemical assays

SARS-CoV-2 M^{pro} residues potentially associated with nirmatrelvir resistance have been identified using a variety of methods, including SARS-CoV-2 resistance selection, testing of recombinant SARS-CoV-2 viruses with M^{pro} substitutions, and biochemical assays with recombinant SARS-CoV-2 M^{pro} containing amino acid substitutions. Table 3 indicates M^{pro} substitutions and combinations of M^{pro} substitutions that have been observed in nirmatrelvir-selected SARS-CoV-2 in cell culture. Individual M^{pro} substitutions are listed regardless of whether they occurred alone or in combination with other M^{pro} substitutions. Note that the M^{pro} S301P and T304I substitutions overlap the P6 and P3 positions of the nsp5/nsp6 cleavage site located at the C-terminus of M^{pro}. Substitutions at other M^{pro} cleavage sites have not been associated with nirmatrelvir resistance in cell culture. The clinical significance of these substitutions is unknown.

Table 3: SARS-CoV-2 M^{pro} amino acid substitutions selected by nirmatrelvir in cell culture

Single substitution (EC_{50} value fold change)	T21I (1.1-4.8), L50F (1.5-4.2), P108S (ND), T135I (ND), F140L (4.1), S144A (2.2-5.3), C160F (ND), E166A (3.3), E166V (25-288), L167F (ND), T169I (ND), H172Y (ND), A173V (0.9-1.7), V186A (ND), R188G (ND), A191V (ND), A193P (ND), P252L (5.9), S301P (ND), and T304I (1.4-5.5).
≥2 substitutions (EC_{50} value fold change)	T21I+S144A (9.4), T21I+E166V (83), T21I+A173V (3.1-8.9), T21I+T304I (3.0-7.9), L50F+E166V (34-175), L50F+T304I (5.9), T135I+T304I (3.8), F140L+A173V (10.1), H172Y+P252L (ND), A173V+T304I (20.2), T21I+L50F+A193P+S301P (28.8), T21I+S144A+T304I (27.8), T21I+C160F+A173V+V186A+T304I (28.5), T21I+A173V+T304I (15), and L50F+F140L+L167F+T304I (54.7).

Abbreviations: ND=no data (substitution emerged from nirmatrelvir resistance selection but has not been tested for EC_{50} determination in an antiviral assay).

In a biochemical assay using recombinant SARS-CoV-2 M^{pro} containing amino acid substitutions, the following SARS-CoV-2 M^{pro} substitutions led to ≥3-fold reduced activity (fold-change based on Ki values) of nirmatrelvir: Y54A (25), F140A (21), F140L (7.6), F140S (230), G143S (3.6), S144A (46), S144E (480), S144T (170), H164N (6.7), E166A (35), E166G (6.2), E166V (7,700), P168del (9.3), H172Y (250), A173V (16), R188G (38), Q192L (29), Q192P (7.8), and V297A (3.0). In addition, the following combinations of Mpro substitutions led to ≥ 3-fold reduced nirmatrelvir activity: T21I+S144A (20), T21I+E166V (11,000), T21I+A173V (15), L50F+E166V (4,500), E55L+S144A (56), T135I+T304I (5.1), F140L+A173V (95), S144A+T304I (28), E166V+L232R (5,700), P168del+A173V (170), H172Y+P252L (180), A173V+T304I (28), T21I+S144A+T304I (51), T21I+A173V+T304I (55), L50F+E166A+L167F (180210), T21I+L50F+A193P+S301P (7.3), L50F+F140L+L167F+T304I (190), and T21I+C160F+A173V+V186A+T304I (28). The following substitutions and substitution combinations emerged in cell culture but conferred <3 fold reduced nirmatrelvir activity in biochemical assays: T21I (1.6), L50F (0.2), P108S (2.9), T135I (2.2), C160F (0.6), L167F (1.5), T169I (1.4), V186A (0.8), A191V (0.8), A193P (0.9), P252L (0.9), S301P

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(0.2), T304I (1.0), T21I+T304I (1.8), and L50F+T304I (1.3). The clinical significance of these substitutions is unknown.

Most single and some double M^{pro} amino and substitutions identified which reduced the susceptibility of SARS-CoV-2 to nirmatrelvir resulted in an EC_{50} shift of <5-fold compared to wild type SARS-CoV-2 in an antiviral cell assay. Virus containing E166V shows the greatest reduction in susceptibility to nirmatrelvir and appears to have replication defect since it either could not be generated or had a very low virus titer. In general, triple and some double M^{pro} amino and substitutions led to EC_{50} changes of >5-fold to that of wild type. The clinical significance needs to be further understood, particularly in the context of nirmatrelvir high clinical exposure (≥5× EC_{90}). Thus far, these substitutions have not been identified as treatment-emergent substitutions associated with hospitalization or death from the EPIC-HR study.

Viral load rebound

Post-treatment increases in SARS-CoV-2 nasal RNA levels (i.e., viral RNA rebound) were observed on Day 10 and/or Day 14 in a subset of PAXLOVID and placebo recipients in EPIC-HR, irrespective of COVID-19 symptoms. The frequency of detection of post-treatment nasal viral RNA rebound varied according to analysis parameters but was generally similar among PAXLOVID and placebo recipients. A similar or smaller percentage of placebo recipients compared to PAXLOVID recipients had nasal viral RNA results < lower limit of quantitation (LLOQ) at all study timepoints in both the treatment and post-treatment periods.

An assessment of treatment-emergent mutations (defined as amino acid substitutions that were absent at baseline and were observed after the start of treatment) was conducted. One substitution, A260T, was observed in a PAXLOVID recipient who experienced hospitalization. The participant with the A260T substitution was hospitalized from Day 2 through Day 8 and the substitution was identified on Day 10 following discharge from the hospital. This substitution has not been identified to be associated with resistance and was not associated with persistence of severe symptoms through Day 28. There were no other treatment-emergent mutations in M^{pro} gene or cleavage targets associated with hospitalization or death or recurrence of increased nasal viral RNA levels post-dose. Post-treatment nasal viral RNA rebounds were not clearly associated with drug resistance as measured using M^{pro} sequencing of SARS-CoV-2 nasal viral RNA. Thus, the clinical relevance of the emergent EPIC-HR M^{pro} gene substitutions remains unclear.

Cross-resistance

Cross-resistance is not expected between nirmatrelvir and remdesivir or any other anti-SARS-CoV-2 agents with different mechanisms of action (i.e., agents that are not M^{pro} inhibitors).

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Pharmacodynamic effects

Cardiac electrophysiology
At 3 times the steady state peak plasma concentration (C_{max}) at the recommended dose, nirmatrelvir does not prolong the QTc interval to any clinically relevant extent.

Effect on lipids
The changes in lipids in nirmatrelvir/ritonavir treated group were not statistically different than placebo/ritonavir treated group in an exploratory analysis of lipids in multiple ascending dose cohorts in which healthy participants were randomized to receive either escalating doses (75, 250 and 500 mg) of nirmatrelvir (n=4 per cohort) or placebo (n=2 per cohort), enhanced with ritonavir 100 mg, twice a day for 10 days.

In participants receiving placebo/ritonavir twice a day, a modest increase in cholesterol (≤ 27.2 mg/dL), LDL cholesterol (≤ 23.2 mg/dL), triglycerides (≤ 64.3 mg/dL) and decrease in HDL cholesterol (≤ 4 mg/dL) was observed. The clinical significance of such changes with short term treatment is unknown.

Clinical efficacy

Efficacy in participants at high risk of progressing to severe COVID-19 illness (EPIC-HR)
The efficacy of PAXLOVID is based on the final analysis of EPIC-HR, a phase 2/3, randomized, double-blind, placebo-controlled study in non-hospitalized symptomatic adult participants with a laboratory confirmed diagnosis of SARS-CoV-2 infection. Eligible participants were 18 years of age and older with at least 1 of the following risk factors for progression to severe disease: diabetes, overweight (BMI >25), chronic lung disease (including asthma), chronic kidney disease, current smoker, immunosuppressive disease or immunosuppressive treatment, cardiovascular disease, hypertension, sickle cell disease, neurodevelopmental disorders, active cancer, medically related technological dependence, or were 60 years of age and older regardless of comorbidities. Participants with COVID-19 symptom onset of ≤ 5 days were included in the study.

Participants were randomized (1:1) to receive PAXLOVID (nirmatrelvir/ritonavir 300 mg/100 mg) or placebo orally every 12 hours for 5 days. The study excluded individuals with a history of prior COVID-19 infection or vaccination. The primary efficacy endpoint was the proportion of participants with COVID-19 related hospitalization or death from any cause through Day 28. Time to sustained alleviation and sustained resolution of all targeted symptoms through Day 28 were key secondary efficacy endpoints. These analyses were conducted in the modified intent-to-treat (mITT) analysis set [all treated participants with onset of symptoms ≤3 days who at baseline did not receive nor were expected to receive COVID-19 therapeutic mAb treatment], the mITT1 analysis set (all treated participants with onset of symptoms ≤5 days who at baseline did not receive nor were expected to receive COVID-19 therapeutic mAb treatment), and the mITT2 analysis set (all treated participants with onset of symptoms ≤5 days).

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A total of 2113 participants were randomized to receive either PAXLOVID or placebo. At baseline, mean age was 45 years; 51% were male; 71% were White, 4% were Black or African American, and 15% were Asian; 41% were Hispanic or Latino; 67% of participants had onset of symptoms ≤3 days before initiation of study treatment; 49% of participants were serological negative at baseline. The mean (SD) baseline viral load was 4.71 $\log_{10}$ copies/mL (2.89); 27% of participants had a baseline viral load of ≥7 $\log_{10}$ copies/mL; 6% of participants either received or were expected to receive COVID-19 therapeutic mAb treatment at the time of randomization and were excluded from the mITT and mITT1 analyses.

The baseline demographic and disease characteristics were balanced between the PAXLOVID and placebo groups.

Table 4 provides results of the primary endpoint in the mITT1 analysis population demonstrating superiority of PAXLOVID compared to placebo for COVID-19 related hospitalization or death from any cause through Day 28. For the primary endpoint, the relative risk reduction in the mITT1 analysis population for PAXLOVID compared to placebo was 86% (95% CI: 72%, 93%).

Table 4: Efficacy results in non-hospitalized adults with COVID-19 dosed within 5 days of symptom onset who did not receive COVID-19 mAb treatment at baseline (mITT1 analysis set)

	PAXLOVID (N=977)	**Placebo** (N=989)
COVID-19 related hospitalization or death from any cause through Day 28		
n (%)	9 (0.9%)	64 (6.5%)
Reduction relative to placebo[a] (95% CI), %	-5.64 (-7.31, -3.97)	
p-value	<0.0001	
All-cause mortality through Day 28, %	0	12 (1.1%)

Abbreviations: CI=confidence interval; COVID-19=Coronavirus Disease 2019; mAb=monoclonal antibody; mITT1=modified intent-to-treat 1 (all participants randomly assigned to study intervention, who took at least 1 dose of study intervention, with at least 1 post-baseline visit through Day 28, who at baseline did not receive nor were expected to receive COVID-19 therapeutic mAb treatment and were treated ≤5 days after COVID-19 symptom onset).
The determination of primary efficacy was based on a planned interim analysis of 754 participants in mITT population. The estimated risk reduction was -6.5% with a 95% CI of (-9.3%, -3.7%) and 2-sided p-value <0.0001.
a. The estimated cumulative proportion of participants hospitalized or death by Day 28 was calculated for each treatment group using the Kaplan-Meier method, where participants without hospitalization and death status through Day 28 were censored at the time of study discontinuation.

Through Week 24, no deaths were reported in the PAXLOVID group compared with 15 deaths in the placebo group. The proportions of participants who discontinued treatment due to an adverse event were 2.0% in the PAXLOVID group and 4.3% in the placebo group.

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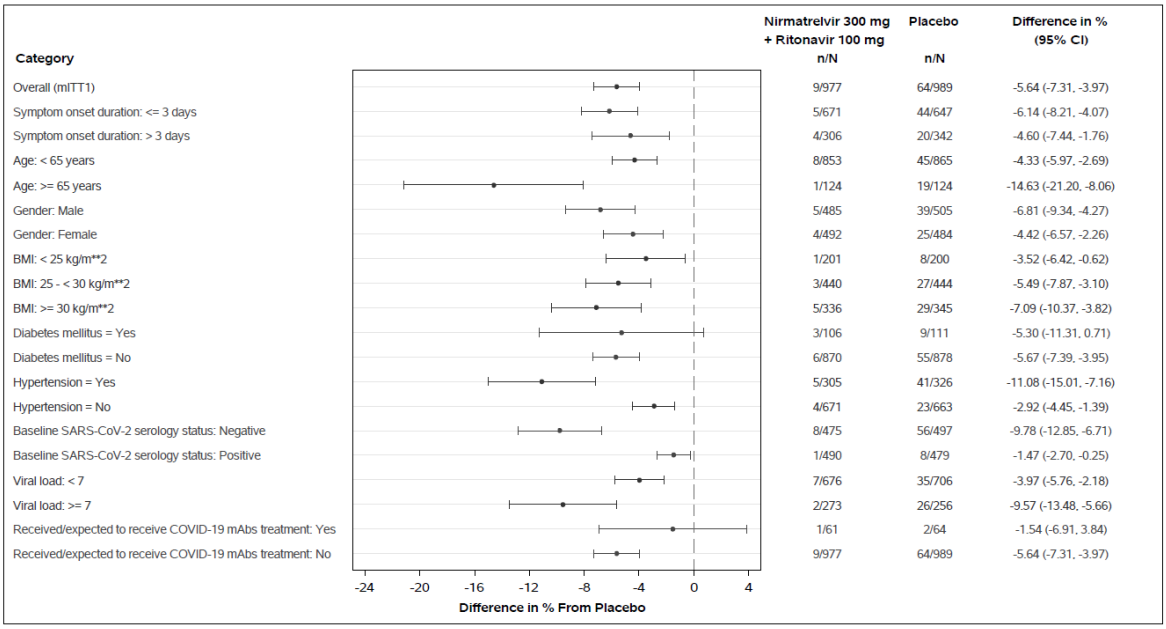
Consistent results were observed in the mITT and mITT2 analysis populations. A total of 1318 participants were included in the mITT analysis population. The event rates were 5/671 (0.75%) in the PAXLOVID group, and 44/647 (6.80%) in the placebo group.

Similar trends have been observed across subgroups of participants (see Figure 1).

Figure 1: Adults with COVID-19 dosed within 5 days of symptom onset with COVID-19-related hospitalization or death from any cause through Day 28



Abbreviations: BMI=body mass index, COVID-19=Coronavirus Disease 2019; mAb=monoclonal antibody; mITT1=modified intent-to-treat 1 (all participants randomly assigned to study intervention, who took at least 1 dose of study intervention, with at least 1 post-baseline visit through Day 28, who at baseline did not receive nor were expected to receive COVID-19 therapeutic mAb treatment and were treated ≤5 days after COVID-19 symptom onset); N=number of participants in the category of the analysis set; SARS-COV-2=severe acute respiratory syndrome coronavirus 2.
All categories are based on mITT1 population except for COVID-19 mAb treatment which is based on mITT2 population.
Seropositivity was defined if results were positive in either Elecsys anti SARS-CoV-2 S or Elecsys SARS-CoV-2 (N) assay.
The difference of the proportions in the 2 treatment groups and its 95% confidence interval based on normal approximation of the data are presented.

Participants performed daily self-assessments of COVID-19 associated symptoms of cough, shortness of breath or difficulty breathing, feeling feverish, chills or shivering, muscle or body aches, diarrhea, nausea, vomiting, headache, sore throat, stuffy or runny nose. The severity of each symptom was rated as absent, mild, moderate, or severe. Sustained symptom alleviation was defined as the first of 4 consecutive days when all of the above symptoms scored as moderate or severe at study entry were scored as mild or absent, and all of the above symptoms scored mild or absent at study entry were scored as absent. Sustained symptom resolution was defined as the time when all of the above symptoms were scored as absent for 4 consecutive days. Table 5 displays the results for time to sustained symptom alleviation and sustained symptom resolution in the mITT1

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population. The PAXLOVID group demonstrated superiority to the placebo group in both analyses.

Table 5: Analyses of Time to Sustained Symptom Alleviation and Sustained Symptom Resolution Through 28 Days (mITT1 Analysis Set): EPIC-HR

	PAXLOVID (N=970)	Placebo (N=986)
Time to sustained symptom alleviation (days)[a]		
Median	13	15
HR vs placebo (95% CI)[b]	1.266 (1.134, 1.412)	
p-value	<0.0001	
Time to sustained symptom resolution (days)[a]		
Median	16	19
HR vs placebo (95% CI)[b]	1.200 (1.068, 1.348)	
p-value	0.0022	

Abbreviations: CI=confidence interval; HR=hazard ratio; COVID-19=Coronavirus Disease 2019; mAb=monoclonal antibody; mITT1=modified intent-to-treat 1 (all participants randomly assigned to study intervention, who took at least 1 dose of study intervention, with at least 1 post-baseline visit through Day 28, who at baseline did not receive nor were expected to receive COVID-19 therapeutic mAb treatment and were treated ≤5 days after COVID-19 symptom onset); SARS-CoV-2=severe acute respiratory syndrome coronavirus 2.

a. Participants who were hospitalized for the treatment of COVID-19 or died during the 28-day period were considered as not achieving sustained symptom alleviation or resolution.
b. Evaluation was done in a Cox proportional hazard model with treatment and geographic region effects as independent variables, and symptom onset duration (≤3, >3 days), baseline SARS-CoV-2 serology status and baseline viral load (<4, ≥4 $\log_{10}$ copies/mL) as covariates.

The proportion of participants with any severe COVID-19 associated symptom was 22% in the PAXLOVID group and 19% in the placebo group at baseline (Day 1), 17% and 18%, respectively, during treatment (from Day 2 to Day 6), and 8% and 11%, respectively, after treatment (from Day 7 to Day 28).

5.2 Pharmacokinetic properties

The pharmacokinetics of nirmatrelvir/ritonavir have been studied in healthy participants and in participants with mild to moderate COVID-19.

Ritonavir is administered with nirmatrelvir as a PK enhancer resulting in higher systemic concentrations and longer half-life of nirmatrelvir. In healthy participants in the fasted state, the mean half-life ($t_{1/2}$) of a single dose of 150 mg nirmatrelvir administered alone was approximately 2 hours compared to 7 hours after administration of a single dose of 250 mg/100 mg nirmatrelvir/ritonavir thereby supporting a twice-daily administration regimen.

Upon administration of single dose of nirmatrelvir/ritonavir 250 mg/100 mg to healthy participants in the fasted state, the geometric mean (CV%) maximum plasma concentration (C_{max}) and area under the plasma concentration-time curve from 0 to the time of last measurement (AUC_{last}) was 2.88 ug/mL (25%) and 27.6 ug*hr/mL (13%), respectively. Upon repeat-dose of nirmatrelvir/ritonavir 75 mg/100 mg, 250 mg/100 mg,

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and 500 mg/100 mg administered twice daily, the increase in systemic exposure at steady-state appears to be less than dose proportional. Multiple dosing over 10 days achieved steady-state on Day 2 with approximately 2-fold accumulation. Systemic exposures on Day 5 were similar to Day 10 across all doses. Simulated repeat-dose exposures of nirmatrelvir/ritonavir 300 mg/100 mg administered twice daily in adult participants from EPIC-HR, suggested the mean AUC_{tau} was 28.3 µg*hr/mL, mean C_{max} was 3.29 µg/mL, and mean C_{min} was 1.40 µg/mL.

Absorption

Following oral administration of nirmatrelvir/ritonavir 300 mg/100 mg after a single dose, the geometric mean nirmatrelvir (CV%) C_{max} and area under the plasma concentration-time curve from 0 to infinity (AUC_{inf}) at steady-state was 2.21 µg/mL (33) and 23.01 µg*hr/mL (23), respectively. The median (range) time to C_{max} (T_{max}) was 3.00 hrs (1.02-6.00). The arithmetic mean (±SD) terminal elimination half-life was 6.1 (1.8) hours.

Following oral administration of nirmatrelvir/ritonavir 300 mg/100 mg after a single dose, the geometric mean ritonavir (CV%) C_{max} and AUC_{inf} was 0.36 µg/mL (46) and 3.60 µg*hr/mL (47), respectively. The median (range) time to C_{max} (T_{max}) was 3.98 hrs (1.48-4.20). The arithmetic mean (±SD) terminal elimination half-life was 6.1 (2.2) hours.

Effect of food on oral absorption
Dosing with a high fat meal increased the exposure of nirmatrelvir (approximately 61% increase in mean C_{max} and 20% increase in mean AUC_{last}) relative to fasting conditions following administration of 300 mg nirmatrelvir (2 × 150 mg)/100 mg ritonavir tablets.

Distribution

The protein binding of nirmatrelvir in human plasma is approximately 69%.

The protein binding of ritonavir in human plasma is approximately 98-99%.

Biotransformation

In vitro studies assessing nirmatrelvir without concomitant ritonavir suggest that nirmatrelvir is primarily metabolized by CYP3A4. Nirmatrelvir is not a substrate of other CYP enzymes. Administration of nirmatrelvir with ritonavir inhibits the metabolism of nirmatrelvir. In human plasma, the only drug-related entity quantifiable was unchanged nirmatrelvir.

In vitro studies utilizing human liver microsomes have demonstrated that cytochrome P450 3A (CYP3A) is the major isoform involved in ritonavir metabolism, although CYP2D6 also contributes to the formation of oxidation metabolite M–2.

Low doses of ritonavir have shown profound effects on the pharmacokinetics of other protease inhibitors (and other products metabolized by CYP3A4) and other protease inhibitors may influence the pharmacokinetics of ritonavir.

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Elimination

The primary route of elimination of nirmatrelvir when administered with ritonavir was renal excretion of intact drug. Approximately 49.6% and 35.3% of the administered dose of nirmatrelvir 300 mg was recovered in urine and feces, respectively. Nirmatrelvir was the predominant drug-related entity with small amounts of metabolites arising from hydrolysis reactions in excreta.

Human studies with radiolabelled ritonavir demonstrated that the elimination of ritonavir was primarily via the hepatobiliary system; approximately 86% of radiolabel was recovered from stool, part of which is expected to be unabsorbed ritonavir.

Special populations

Age and gender
The pharmacokinetics of nirmatrelvir/ritonavir based on age and gender have not been evaluated.

Pediatric patients
The pharmacokinetics of nirmatrelvir/ritonavir in pediatric patients have not been evaluated.

Racial or ethnic groups
Systemic exposure in Japanese participants was numerically lower but not clinically meaningfully different than those in Western participants.

Patients with renal impairment
Compared to healthy controls with no renal impairment, the C_{max} and AUC_{inf} of nirmatrelvir in participants with mild renal impairment were 30% and 24% higher, in patients with moderate renal impairment were 38% and 87% higher, and in participants with severe renal impairment were 48% and 204% higher, respectively.

Patients with hepatic impairment
Compared to healthy controls with no hepatic impairment, the pharmacokinetics of nirmatrelvir in participants with moderate hepatic impairment were not significantly different. Adjusted geometric mean ratio (90% CI) of AUC_{inf} and C_{max} of nirmatrelvir comparing moderate hepatic impairment (test) to normal hepatic function (reference) were 98.78% (70.65%, 138.12%) and 101.96% (74.20%, 140.11%), respectively.

Nirmatrelvir/ritonavir has not been studied in patients with severe hepatic impairment.

Drug interaction studies conducted with nirmatrelvir

In vitro data indicates that nirmatrelvir is a substrate for human MDR1 (P-gp) and CYP3A4, but not a substrate for human BCRP, MATE1, MATE2K, NTCP, OAT1, OAT2, OAT3, OCT1, OCT2, PEPT1, OATPs 1B1, 1B3, 2B1, or 4C1.

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Nirmatrelvir does not reversibly inhibit CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, or CYP2D6 in vitro at clinically relevant concentrations. Nirmatrelvir has the potential to reversibly and time dependently inhibit CYP3A4 and inhibit MDR1 (P-gp) and OATP1B1.

Nirmatrelvir does not induce any CYPs at clinically relevant concentrations.

Drug interaction studies conducted with nirmatrelvir/ritonavir

In vitro studies indicate that ritonavir is mainly a substrate of CYP3A. Ritonavir also appears to be a substrate of CYP2D6 which contributes to the formation of isopropylthiazole oxidation metabolite M-2.

Ritonavir is an inhibitor of CYP3A and to a lesser extent CYP2D6. Ritonavir appears to induce CYP3A, CYP1A2, CYP2C9, CYP2C19, and CYP2B6 as well as other enzymes, including glucuronosyl transferase.

The effects of co-administration of PAXLOVID with itraconazole (CYP3A inhibitor) and carbamazepine (CYP3A inducer) on the nirmatrelvir AUC and C_{max} are summarized in Table 6.

Table 6: Effect of co-administered drugs on pharmacokinetics of nirmatrelvir

Co-administered drug	Dose (schedule)		N	Percent ratio of nirmatrelvir[a] PK parameters (90% CI); no effect=100	
	Co-administered	Nirmatrelvir/ ritonavir		C_{max}	AUC[b]
Carbamazepine[c]	300 mg twice daily (16 doses)	300 mg/100 mg once daily (2 doses)	10	56.82 (47.04, 68.62)	44.50 (33.77, 58.65)
Itraconazole	200 mg once daily (8 doses)	300 mg/100 mg twice daily (5 doses)	11	118.57 (112.50, 124.97)	138.82 (129.25, 149.11)

Abbreviations: AUC=area under the plasma concentration-time curve; CI=confidence interval; C_{max}=observed maximum plasma concentrations; PK=pharmacokinetic.
a. Percent ratio of test (i.e., carbamazepine or itraconazole in combination with nirmatrelvir/ritonavir)/reference (i.e., nirmatrelvir/ritonavir alone).
b. For carbamazepine, AUC=AUC_{inf}; for itraconazole, AUC=AUC_{tau}.
c. Carbamazepine titrated up to 300 mg twice daily on Day 8 through Day 15 (e.g., 100 mg twice daily on Day 1 through Day 3 and 200 mg twice daily on Day 4 through Day 7).

The effects of co-administration of PAXLOVID with midazolam (CYP3A4 substrate), dabigatran (P-gp substrate), or rosuvastatin (OATP1B1 substrate) on the midazolam, dabigatran, and rosuvastatin AUC_{inf} and C_{max}, respectively, are summarized in Table 7.

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Table 7: Effect of nirmatrelvir/ritonavir on pharmacokinetics of co-administered drug

Co-administered drug	Dose (schedule)		N	Percent ratio[a] of test/reference of geometric means (90% CI); no effect=100	
	Co-administered	Nirmatrelvir/ ritonavir		C_{max}	AUC_{inf}
Midazolam[b]	2 mg (1 dose)	300 mg/100 mg twice daily (9 doses)	10	368.33 (318.91, 425.41)	1430.02 (1204.54, 1697.71)
Dabigatran[b]	75 mg (1 dose)	300 mg/100 mg twice daily (4 doses)	24	233.06 (172.14, 315.54)	194.47 (155.29, 243.55)
Rosuvastatin[b]	10 mg (1 dose)	300 mg/100 mg twice daily (3 doses)	12	212.44 (174.31, 258.90)	131.18 (115.89, 148.48)

Abbreviations: AUC_{inf}=area under the plasma concentration-time curve from time 0 to infinity; CI=confidence interval; C_{max}=maximum plasma concentrations; CYP3A4=cytochrome P450 3A4; OATP1B1=organic anion transporting polypeptide 1B1; P-gp=p-glycoprotein.
a. Percent ratio of test (i.e., midazolam, dabigatran or rosuvastatin in combination with nirmatrelvir/ritonavir)/reference (i.e., midazolam, dabigatran, or rosuvastatin alone).
b. For midazolam, Test=nirmatrelvir/ritonavir plus midazolam, Reference=midazolam. Midazolam is an index substrate for CYP3A4. For dabigatran, Test=nirmatrelvir/ritonavir plus dabigatran, Reference=dabigatran. Dabigatran is an index substrate for P-gp. For rosuvastatin, Test=nirmatrelvir/ritonavir plus rosuvastatin, Reference=rosuvastatin. Rosuvastatin is an index substrate for OATP1B1.

5.3 Pre-clinical safety data

Toxicology

Repeat-dose toxicity studies up to 1 month duration of nirmatrelvir in rats and monkeys resulted in no adverse findings.

Repeat-dose toxicity studies of ritonavir in animals identified major target organs as the liver, retina, thyroid gland, and kidney. Hepatic changes involved hepatocellular, biliary, and phagocytic elements and were accompanied by increases in hepatic enzymes. Hyperplasia of the retinal pigment epithelium and retinal degeneration have been seen in all of the rodent studies conducted with ritonavir, but have not been seen in dogs. Ultrastructural evidence suggests that these retinal changes may be secondary to phospholipidosis. However, clinical trials revealed no evidence of drug-induced ocular changes in humans. All thyroid changes were reversible upon discontinuation of ritonavir. Clinical investigation in humans has revealed no clinically significant alteration in thyroid function tests.

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Renal changes including tubular degeneration, chronic inflammation and proteinuria were noted in rats and are considered to be attributable to species-specific spontaneous disease. Furthermore, no clinically significant renal abnormalities were noted in clinical trials.

Carcinogenesis

Nirmatrelvir has not been evaluated for the potential to cause carcinogenicity.

Long-term carcinogenicity studies of ritonavir in mice and rats revealed tumorigenic potential specific for these species, but are regarded as of no relevance for humans.

Genotoxicity

Nirmatrelvir was not genotoxic in a battery of assays, including bacterial mutagenicity, chromosome aberration using human lymphoblastoid TK6 cells and *in vivo* rat micronucleus assays.

Ritonavir was found to be negative for mutagenic or clastogenic activity in a battery of *in vitro* and *in vivo* assays including the Ames bacterial reverse mutation assay using *S. typhimurium* and *E. coli*, the mouse lymphoma assay, the mouse micronucleus test, and chromosomal aberration assays in human lymphocytes.

Reproductive toxicity

Nirmatrelvir
In a fertility and early embryonic development study, nirmatrelvir was administered to male and female rats by oral gavage at doses of 60, 200, or 1,000 mg/kg/day once daily beginning 14 days prior to mating, throughout the mating phase, and continued through Gestation Day (GD) 6 for females and for a total of 32 doses for males. There were no effects on fertility, reproductive performance, or early embryonic development at doses up to 1,000 mg/kg/day representing 12x/4.3x based on the predicted human C_{max}/AUC_{24} at a twice-daily dose of 300 mg/100 mg nirmatrelvir/ritonavir.

The potential embryo-foetal toxicity of nirmatrelvir was evaluated in the definitive rat and rabbit studies at doses up to 1,000 mg/kg/day. There was no nirmatrelvir-related effect in any of the parameters in the rat embryo-foetal development (EFD) study up to the highest dose of 1,000 mg/kg/day (exposure margin of 16x/7.8x based on total C_{max}/AUC_{24} over the predicted human exposures at a dose of 300 mg/100 mg nirmatrelvir/ritonavir twice daily).

In the rabbit EFD study, there was no nirmatrelvir-related effect on foetal morphology or embryo-foetal viability up to the highest dose of 1,000 mg/kg/day (exposure margin of 24x/10x based on total C_{max}/AUC_{24}), however adverse nirmatrelvir-related lower foetal body weights (0.91x control) were observed at 1,000 mg/kg/day in the presence of nonadverse, low magnitude effects on maternal body weight change and food consumption at this dose. Growth delay is likely reversible following cessation of exposure in human, and it was not present at the intermediate dose (10x/2.8x C_{max}/AUC_{24} over the predicted clinical exposure). There were no nirmatrelvir-related severe

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manifestations of developmental toxicity (malformations and embryo-foetal lethality) at the highest dose tested 1,000 mg/kg/day.

Ritonavir
Ritonavir produced no effects on fertility in rats.

Ritonavir was administered orally to pregnant rats (at 0, 15, 35, and 75 mg/kg/day) and rabbits (at 0, 25, 50, and 110 mg/kg/day) during organogenesis (on GD 6 through 17 in rats and GD 6 through 19 in rabbits). No evidence of teratogenicity due to ritonavir was observed in rats and rabbits at systemic exposures (AUC) 5× (rats) or 8× (rabbits) higher than exposure at the approved human dose of PAXLOVID. Increased incidences of early resorptions, ossification delays, and developmental variations, as well as decreased fetal body weights were observed in rats in the presence of maternal toxicity, at systemic exposures approximately 10× higher than exposure at the approved human dose of PAXLOVID. In rabbits, resorptions, decreased litter size, and decreased fetal weights were observed at maternally toxic doses, at systemic exposures greater than 8× higher than exposure at the approved human dose of PAXLOVID. In a pre- and postnatal development study in rats, administration of 0, 15, 35, and 60 mg/kg/day ritonavir from GD 6 through Postnatal Day 20 resulted in no developmental toxicity, at ritonavir systemic exposures greater than10× the exposure at the approved human dose of PAXLOVID.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Nirmatrelvir
Tablet core:
Microcrystalline cellulose
Lactose monohydrate
Croscarmellose sodium
Colloidal silicon dioxide
Sodium stearyl fumarate
Film-coat:
Hypromellose (E464)
Titanium dioxide (E171)
Macrogol (E1521)
Iron oxide red (E172)

Ritonavir
Tablet core:
Copovidone
Sorbitan laurate
Silica colloidal anhydrous (E551)
Calcium hydrogen phosphate anhydrous
Sodium stearyl fumarate
Film-coat:

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Hypromellose (E464)
Titanium dioxide (E171)
Macrogol (E1521)
Hydroxypropyl cellulose (E463)
Talc (E553b)
Silica colloidal anhydrous (E551)
Polysorbate 80 (E433)

6.2 Incompatibilities

Not applicable.

6.3 Special precautions for storage

Store below 30 °C.
Do not refrigerate or freeze.

6.4 Nature and contents of container

Box of 5 blisters @ 4 Nirmatrelvir 150 mg Film-coated Tablets and 2 Ritonavir 100 mg Film-coated Tablets.

6.5 Special precautions for disposal

No special requirements for disposal.

7. MARKETING AUTHORISATION HOLDER

Nirmatrelvir Film-coated Tablet, manufactured by:
Pfizer Manufacturing Deutschland GmbH
Freiburg, Germany

Ritonavir Film-coated Tablet, manufactured by:
Hetero Labs Limited
Hyderabad, India

Packed and released by:
Pfizer Italia S.r.l.
Ascoli Piceno, Italy

Imported by:
PT. Pfizer Indonesia
Jakarta, Indonesia

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8. MARKETING AUTHORISATION NUMBER(S)

Reg. No DKI2354201217A1

9. DATE OF REVISION OF THE TEXT

10/2025

HARUS DENGAN RESEP DOKTER

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Leaflet kemasan: Informasi untuk pasien

PAXLOVID

Nirmatrelvir 150 mg/Ritonavir 100 mg tablet salut selaput

Baca semua bagian leaflet ini dengan cermat sebelum mulai menggunakan obat ini karena berisi informasi penting bagi Anda.

- Simpan leaflet ini. Anda mungkin perlu membacanya kembali.
- Jika Anda memiliki pertanyaan lebih lanjut, tanyakan kepada dokter, apoteker, atau perawat Anda.
- Obat ini telah diresepkan hanya untuk Anda. Jangan memberikannya kepada orang lain. Obat ini dapat membahayakan mereka, sekalipun tanda-tanda penyakit mereka sama dengan Anda.
- Jika Anda mengalami efek samping apa pun, konsultasikan dengan dokter atau perawat Anda. Termasuk setiap kemungkinan efek samping yang tidak tercantum dalam leaflet ini. Lihat bagian 13.

Isi leaflet ini:

1. Nama obat

PAXLOVID

2. Bentuk sediaan

Tablet salut selaput

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3. Deskripsi obat

Nirmatrelvir tablet salut selaput
Tablet salut selaput berbentuk lonjong berwarna merah muda dengan tulisan PFE di satu sisi dan 3CL di sisi sebaliknya.

Ritonavir tablet salut selaput
Tablet salut selaput berbentuk kapsul dengan warna putih hingga hampir putih, dengan tulisan 'H' di satu sisi dan 'R9' di sisi sebaliknya.

4. Apa kandungan obat ini?

PAXLOVID adalah tablet nirmatrelvir yang dikemas bersama tablet ritonavir.

Setiap tablet salut selaput nirmatrelvir berwarna merah muda mengandung 150 mg nirmatrelvir.

Setiap tablet salut selaput ritonavir berwarna putih muda mengandung 100 mg ritonavir.

Eksipien:
Nirmatrelvir
Inti tablet:
Mikrokristalin selulosa
Laktosa monohidrat
Kroskarmelosa natrium
Koloidal silikon dioksida
Natrium stearil fumarat
Salut selaput:
Hipromelosa (E464)
Titanium dioksida (E171)
Makrogol (E1521)
Besi oksida merah (E172)

Ritonavir
Inti tablet:
Kopovidon
Sorbitan laurat
Silika koloidal anhidrat (E551)
Kalsium hidrogen fosfat anhidrat
Natrium stearil fumarat
Salut selaput:
Hipromelosa (E464)
Titanium dioksida (E171)
Makrogol (E1521)
Hidroksipropil selulosa (E463)
Talk (E553b)
Silika koloidal anhidrat (E551)
Polisorbat 80 (E433)

5. Kekuatan obat

Nirmatrelvir 150 mg dan ritonavir 100 mg tablet salut selaput.

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6. Apa kegunaan obat ini?

Apa itu Paxlovid?

Obat ini digunakan untuk mengobati COVID-19 pada orang dewasa yang tidak parah dan tidak memerlukan oksigen tambahan, serta yang berisiko tinggi mengalami perkembangan penyakit menuju COVID- 19 berat.

COVID-19 disebabkan oleh virus. Paxlovid menghentikan multiplikasi virus di dalam sel sehingga akan menghentikan multiplikasi virus di dalam tubuh. Mekanisme ini dapat membantu tubuh Anda memerangi infeksi virus sehingga diharapkan kondisi Anda membaik lebih cepat.

Paxlovid mengandung zat aktif nirmatrelvir dan ritonavir. Nirmatrelvir adalah zat aktif yang melawan virus penyebab COVID-19. Ritonavir memperpanjang efek terapeutik nirmatrelvir.

Kondisi kesehatan yang dikaitkan dengan peningkatan risiko berkembangnya penyakit berat akibat COVID-19 antara lain:

• Usia ⩾ 60 tahun
• BMI > 25
• Perokok aktif dan memiliki riwayat minimal pernah mengisap 100 batang rokok
• Penyakit imunosupresif atau penggunaan obat-obatan yang melemahkan sistem imun untuk waktu yang lama
• Penyakit paru kronis
• Penyakit kardiovaskular
• Diabetes melitus tipe 1 atau 2
• Penyakit ginjal kronis
• Penyakit sel bulan sabit
• Penyakit perkembangan syaraf
• Penyakit kanker
• Pengobatan yang bergantung pada alat (misalnya, terapi pemberian aliran udara ke saluran pernafasan [tidak terkait dengan COVID-19])

Anda harus berkonsultasi dengan dokter jika kondisi Anda tidak kunjung membaik atau bertambah buruk selama menjalani pengobatan dengan Paxlovid.

7. Berapa banyak dan seberapa sering Anda seharusnya menggunakan obat ini? Apa yang harus dilakukan jika ada dosis yang terlewat?

Selalu gunakan obat ini dengan tepat sesuai petunjuk dokter Anda. Tanyakan kepada dokter atau perawat Anda jika Anda merasa tidak yakin.

PAXLOVID terdiri dari 2 obat: nirmatrelvir dan ritonavir. Dosis yang dianjurkan adalah 2 tablet nirmatrelvir dengan 1 tablet ritonavir yang diminum dua kali sehari (pada pagi hari dan malam hari).

Satu rangkaian pengobatan berlangsung selama 5 hari. Untuk setiap dosis, minum ketiga tablet bersamaan pada waktu yang sama.

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Telan tablet secara utuh. Jangan mengunyah, mematahkan, atau menggerus tablet. PAXLOVID dapat diminum sebelum atau sesudah makan.

Penggunaan pada pasien gangguan ginjal
Jika Anda menderita penyakit ginjal, konsultasikan dengan petugas kesehatan untuk mengetahui dosis PAXLOVID yang sesuai. Jika Anda menderita penyakit ginjal sedang, dosis PAXLOVID Anda akan perlu diturunkan**, harap ikuti perintah dokter Anda dengan hati-hati, karena jumlah tablet yang Anda butuhkan mungkin lebih sedikit daripada jumlah yang ada dalam kemasan obat**. Jika Anda menderita penyakit ginjal berat, Anda dilarang meminum Paxlovid.

Penggunaan pada anak-anak dan remaja
PAXLOVID tidak digunakan untuk mengobati anak-anak dan remaja (usia di bawah 18 tahun).

Jika Anda lupa meminum PAXLOVID
Jika Anda lupa untuk meminum satu dosis PAXLOVID, minum sesegera mungkin setelah Anda ingat. Jika lebih dari 8 jam telah berlalu sejak dosis Anda yang terlewat, jangan meminum dosis yang terlewat tersebut dan lanjutkan dosis berikutnya sebagaimana mestinya.

Jangan meminum dosis ganda untuk menggantikan dosis yang terlupa.

Jika Anda merasa lebih baik
Jika Anda merasa lebih baik, jangan menghentikan penggunaan PAXLOVID tanpa berkonsultasi dengan petugas kesehatan Anda.

Jika Anda memiliki pertanyaan lebih lanjut seputar penggunaan obat ini, tanyakan kepada dokter atau apoteker Anda.

8. Kapan seharusnya Anda tidak menggunakan obat ini?

Jangan gunakan PAXLOVID:

- jika Anda alergi terhadap nirmatrelvir, ritonavir, atau bahan lain yang terkandung dalam PAXLOVID (tercantum di bagian 6).
- jika Anda sedang menggunakan obat-obatan berikut ini. Menggunakan PAXLOVID bersama obat-obatan ini dapat menimbulkan efek samping yang serius dan mengancam jiwa atau memengaruhi cara kerja PAXLOVID:
  - alfuzosin (digunakan untuk mengobati gejala-gejala pembesaran prostat)
  - petidin, piroksikam, propoksifen (digunakan untuk meredakan nyeri)
  - apalutamid, enzalutamid, neratinib, venetoclax (digunakan untuk mengobati kanker)
  - ranolazine (digunakan untuk mengobati nyeri dada kronis [angina])
  - amiodaron, bepridil, dronedaron, encainide, flecainide, propafenon, kuinidin (digunakan untuk mengobati gangguan jantung dan mengatasi detak jantung tidak teratur)
  - asam fusidat, rifampisin, rifapentine (digunakan untuk mengobati infeksi bakteri)
  - karbamazepin, fenobarbital, primidon, fenitoin (digunakan untuk mencegah dan mengendalikan kejang)
  - kolkisin (digunakan untuk mengobati encok)
  - astemizol, terfenadin (digunakan untuk mengobati alergi)
  - lurasidon (digunakan untuk mengobati skizofrenia)

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- pimozid, klozapin, quetiapine (digunakan untuk mengobati skizofrenia, kelainan bipolar, depresi berat, serta pemikiran atau perasaan yang tidak normal)
- silodosin (digunakan untuk mengobati pembesaran kelenjar prostat)
- eplerenon dan ivabradin (digunakan untuk mengobati gangguan jantung dan/atau pembuluh darah)
- dihidroergotamin dan ergotamin (digunakan untuk mengobati sakit kepala karena migrain)
- ergonovin dan metilergonovin (digunakan untuk menghentikan perdarahan berlebih yang mungkin terjadi setelah persalinan atau aborsi)
- cisapride (digunakan untuk meredakan gangguan lambung tertentu)
- St. John's wort (*Hypericum perforatum*) (obat herbal yang digunakan untuk depresi dan kecemasan)
- voklosporin (digunakan untuk mengobati kelainan imun)
- lovastatin, simvastatin, lomitapid (digunakan untuk menurunkan kolesterol darah)
- eletriptan, ubrogepant (digunakan untuk mengobati sakit kepala karena migrain)
- avanafil, vardenafil (digunakan untuk mengobati disfungsi ereksi [dikenal juga dengan istilah impotensi])
- sildenafil (Revatio®) (digunakan untuk mengobati hipertensi arteri paru [tekanan darah tinggi pada arteri paru])
- klonazepam, diazepam, estazolam, flurazepam, triazolam, midazolam yang digunakan secara oral (digunakan untuk meredakan kecemasan dan/atau gangguan tidur)
- tolvaptan yang digunakan untuk mengobati hiponatremia (kadar natrium rendah dalam darah)
- finerenone
- suzetrigine (digunakan untuk membantu mengelola nyeri)
- naloxegol
- flibanserin
- rifampin (digunakan untuk mengobati tuberkulosis)
- lumacaftor, ivacaftor

9. Apa yang harus dipertimbangkan saat menggunakan obat ini?

Konsultasikan dengan dokter Anda sebelum meminum PAXLOVID.

Reaksi alergi

Reaksi alergi, termasuk reaksi alergi berat (disebut dengan istilah 'anafilaksis'), dan reaksi alergi serius (dikenal dengan istilah nekrolisis epidermal toksik dan sindrom Stevens-Johnson) dapat dialami oleh orang-orang yang meminum PAXLOVID, sekali pun hanya 1 dosis. Hentikan meminum PAXLOVID dan hubungi dokter Anda secepatnya jika Anda mengalami gejala reaksi alergi mana pun berikut ini:

- kesulitan menelan atau bernapas
- pembengkakan lidah, mulut, dan wajah
- tenggorokan terasa ketat
- suara parau
- gatal-gatal
- ruam kulit
- kulit memerah dan nyeri
- kulit melepuh dan mengelupas
- lepuh atau luka pada mulut atau bibir Anda

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Penyakit hati
Beri tahu dokter Anda jika Anda menderita atau pernah menderita penyakit hati. Enzim hati yang abnormal, hepatitis, dan penyakit kuning telah muncul pada pasien yang menerima ritonavir.

Penyakit ginjal
Beri tahu dokter Anda jika Anda menderita atau pernah menderita penyakit ginjal.

Risiko berkembangnya resistansi HIV-1
Jika Anda mengalami infeksi HIV yang tidak diobati atau tidak terkontrol, PAXLOVID dapat menyebabkan sebagian obat-obatan HIV tidak dapat bekerja dengan baik di kemudian hari.

Pasien anak-anak dan remaja
Jangan memberikan PAXLOVID kepada anak-anak dan remaja di bawah 18 tahun karena penggunaan PAXLOVID pada anak-anak dan remaja belum diteliti.

PAXLOVID mengandung laktosa
Jika Anda telah diberi tahu oleh dokter bahwa Anda mempunyai intoleransi terhadap jenis gula tertentu, hubungi dokter Anda sebelum menggunakan obat ini.

PAXLOVID mengandung natrium
Tablet nirmatrelvir dan ritonavir sama-sama mengandung kurang dari 1 mmol natrium (23 mg) per dosis, sehingga pada dasarnya bisa dikatakan ‘bebas natrium’.

10. Apa saja obat lain yang harus dihindari selama menggunakan obat ini?

Beri tahu dokter atau apoteker Anda jika Anda sedang, belum lama ini, atau mungkin akan menggunakan obat lain.

- obat-obatan yang digunakan untuk mengobati kanker, seperti afatinib, abemaciclib, apalutamid, enzalutamid, seritinib, dasatinib, encorafenib, fostamatinib, ibrutinib, ivosidenib, nilotinib, vinblastin, dan vinkristin
- obat-obatan yang digunakan untuk mengencerkan darah (antikoagulan atau antiplatelet), seperti ticagrelor, warfarin, rivaroksaban, vorapaxar, apiksaban, dan dabigatran
- obat-obatan yang digunakan untuk berhenti merokok, seperti bupropion
- obat-obatan yang digunakan untuk mengobati alergi, seperti feksofenadin dan loratadin
- obat-obatan yang digunakan untuk mengatasi infeksi jamur (antijamur), seperti isavukonazonium sulfat, itrakonazol, dan vorikonazol
- obat-obatan yang digunakan untuk mengobati infeksi parasit, seperti albendazolobat-obatan yang digunakan untuk mengobati sindrom Cushing—saat tubuh memproduksi kortisol secara berlebih—seperti tablet ketokonazol
- obat-obatan yang digunakan untuk mengobati infeksi HIV seperti efavirenz, maraviroc, raltegravir, dan zidovudin
- obat-obatan yang digunakan untuk mengobati infeksi (misalnya antibiotik dan antimikobakteri), seperti atovaquone, klaritromisin, eritromisin, bedakuilin, rifabutin, delamanid, dan sulfametoksazol/trimetoprim
- obat-obatan yang digunakan untuk mengobati tekanan darah tinggi pada pembuluh darah yang mengalir ke paru-paru, seperti bosentan dan riociguat
- obat-obatan yang digunakan untuk mengobati tekanan darah tinggi (hipertensi), seperti amlodipin, diltiazem, felodipin, nikardipin, verapamil, nifedipin dan aliskiren

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- obat-obatan yang digunakan untuk mengobati gangguan jantung dan mengoreksi detak jantung tidak teratur, seperti digoksin, lidokain (sistemik), disopiramid dan mavacamten
- obat-obatan yang digunakan untuk mengobati infeksi virus hepatitis C, seperti glecaprevir/pibrentasvir
- obat-obatan yang digunakan untuk menurunkan kolesterol darah, seperti atorvastatin, fluvastatin, pravastatin, dan rosuvastatin
- obat-obatan yang digunakan untuk menekan sistem kekebalan tubuh Anda, seperti siklosporin, everolimus, sirolimus, dan takrolimus
- obat-obatan yang digunakan untuk mengobati nyeri berat, seperti morfin, fentanil, metadon, buprenorpin, obat-obatan menyerupai morfin lainnya
- obat-obatan yang digunakan untuk mengobati nyeri tetapi bukan obat-obatan menyerupai morfin, misalnya suzetrigine
- obat-obatan yang digunakan sebagai sedatif, hipnotik, dan obat tidur, seperti alprazolam, buspiron, dan zolpidem
- steroid termasuk kortikosteroid yang digunakan untuk mengobati inflamasi, seperti betametason, budesonid, siklesonid, deksametason, flutikason, prednisolon, metilprednisolon, mometason, dan triamsinolon
- obat-obatan yang digunakan untuk mengobati asma dan gangguan paru-paru lainnya seperti penyakit paru obstruktif kronis [PPOK], misalnya salmeterol dan teofilin
- obat-obatan yang digunakan untuk mengobati depresi, seperti amitriptilin, fluoksetin, imipramin, nortriptilin, trazodon, paroksetin, dan sertralin
- obat-obatan yang digunakan sebagai terapi penggantian tiroid, seperti levotiroksin
- obat-obatan yang digunakan untuk mengobati gangguan perhatian, seperti turunan amfetamin, misalnya metilfenidat dan deksafetamin
- ivacaftor, elexacaftor, atau tezacaftor
- tamsulosin
- obat-obatan yang digunakan untuk mengobati diabetes tipe 2, seperti saksagliptin
- tofasitinib, upadasitinib
- rimegepant
- darifenasin
- aripiprazole, brekspiprazol, cariprazine, iloperidone, lumateperone, pimavanserin

Obat-obatan spesifik lainnya, sebagai berikut ini:

- obat kontrasepsi oral atau koyok yang mengandung etinil estradiol yang digunakan untuk mencegah kehamilan
- midazolam yang diberikan melalui injeksi (digunakan untuk sedasi [kondisi terjaga, tetapi sangat rileks dan tenang atau mengantuk selama pemeriksaan atau prosedur medis] atau pembiusan)

Banyak obat-obatan yang berinteraksi dengan PAXLOVID. **Simpan daftar obat-obatan Anda untuk diperlihatkan kepada dokter atau apoteker.** Jangan mulai meminum obat-obatan baru tanpa berkonsultasi dengan dokter Anda. Dokter Anda dapat memberi tahu Anda apakah PAXLOVID aman digunakan bersama obat-obatan lainnya.

11. Apakah obat ini aman untuk ibu hamil dan menyusui?

Jika Anda hamil, menduga bahwa diri Anda hamil, atau sedang merencanakan kehamilan, mintalah saran dari dokter Anda sebelum menggunakan obat ini.

Tidak terdapat cukup informasi untuk memastikan bahwa PAXLOVID aman digunakan selama kehamilan. Jika Anda sedang hamil, tidak disarankan menggunakan PAXLOVID kecuali kondisi klinis Anda mengharuskan pengobatan ini.

Disarankan agar Anda berpantang dari aktivitas seksual atau menggunakan metode kontrasepsi selama meminum PAXLOVID dan hingga 7 hari setelah menyelesaikan pengobatan dengan PAXLOVID sebagai tindakan pencegahan. Karena PAXLOVID dapat mengurangi efektivitas kontrasepsi hormonal, maka selama penggunaannya Anda disarankan untuk menggunakan pula kondom atau metode kontrasepsi nonhormonal lainnya. Dokter akan memberi tahu Anda mengenai durasi yang diperlukan untuk penyesuaian metode kontrasepsi ini.

Sejumlah kecil PAXLOVID masuk ke dalam ASI. Sebagai tindakan pencegahan, Anda tidak boleh menyusui bayi Anda selama menggunakan PAXLOVID dan dalam 48 jam setelah menyelesaikan pengobatan dengan PAXLOVID.

12. Apakah pasien diperbolehkan mengemudi dan mengoperasikan mesin selama menggunakan obat ini?
PAXLOVID belum diuji secara spesifik untuk kemungkinan efeknya terhadap kemampuan mengemudi atau mengoperasikan mesin.

13. Apa saja potensi efek yang tidak diinginkan dari penggunaan obat ini?
Seperti obat-obatan lainnya, obat ini dapat menimbulkan efek samping, sekalipun tidak semua orang mengalaminya.

Umum: dapat dialami oleh 1 di antara 10 orang
- Diare
- Mual
- Perubahan indra perasa
- Sakit kepala

Tidak umum: dapat dialami oleh 1 di antara 100 orang
- Reaksi alergi (seperti gatal-gatal atau ruam kulit)
- Tekanan darah tinggi
- Muntah
- Sakit perut

Jarang: dapat dialami oleh 1 di antara 1000 orang
- Reaksi alergi berat yang dikenal dengan istilah ‘anafilaksis’ (seperti pembengkakan lidah, mulut, dan wajah, kesulitan menelan atau bernapas, tenggorokan seperti tercekik, atau suara parau)
- Reaksi kulit serius yang dikenal dengan istilah ‘nekrolisis epidermal toksik’ dan ‘Sindrom Stevens-Johnson’ (seperti kulit memerah dan nyeri, kulit melepuh dan terkelupas, terdapat lepuh atau luka pada mulut atau bibir Anda)
- Malaise

Melaporkan efek samping
Jika Anda mengalami efek samping apa pun, konsultasikan dengan dokter atau perawat Anda. Termasuk setiap kemungkinan efek samping yang tidak tercantum dalam leaflet ini. Dengan

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melaporkan efek samping, Anda bisa membantu memberikan informasi lebih banyak mengenai keamanan obat ini.

Untuk melaporkan efek samping, hubungi www.pfizersafetyreporting.com atau email di IDN.AEReporting@pfizer.com.

14. Tanda-tanda dan gejala-gejala overdosis
Pengobatan overdosis PAXLOVID sebaiknya terdiri dari tindakan suportif umum termasuk pemantauan tanda-tanda vital dan observasi status klinis pasien. Tidak ada penawar yang spesifik untuk overdosis PAXLOVID.

15. Apa yang harus dilakukan jika Anda menggunakan lebih dari dosis yang dianjurkan?
Jika Anda terlalu banyak meminum dosis PAXLOVID, hubungi penyedia layanan kesehatan Anda atau kunjungi unit gawat darurat di rumah sakit terdekat secepatnya.

16. Bagaimana cara menyimpan obat ini?
Simpan pada suhu di bawah 30 °C.

Jangan disimpan di lemari pendingin atau dibekukan.

Jauhkan obat ini dari pandangan dan jangkauan anak-anak.

Jangan gunakan obat ini setelah melewati tanggal kedaluwarsa yang tertera pada wadahnya.

17. Nomor izin edar
Box dari 5 blister @ 4 Nirmatrelvir 150 mg Tablet salut selaput dan 2 Tablet salut selaput Ritonavir 100 mg. No. Reg: DKI2354201217A1

18. Nama dan alamat pemohon dan/atau pemilik obat sesuai dengan ketentuan yang berlaku

Nirmatrelvir Tablet Salut Selaput, diproduksi oleh:
Pfizer Manufacturing Deutschland GmbH
Freiburg, Jerman

Ritonavir Tablet Salut Selaput, diproduksi oleh:
Hetero Labs Limited
Hyderabad, India

Dikemas dan diedarkan oleh:
Pfizer Italia S.r.l.
Ascoli Piceno, Italia

Diimpor oleh:
PT. Pfizer Indonesia
Jakarta, Indonesia

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19. Tanggal revisi

10/2025

HARUS DENGAN RESEP DOKTER

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