PAXLOVID™
(nirmatrelvir 150 mg tablets | ritonavir 100 mg tablets)

Dosing & Prescribing Reference Guide

PAXLOVID has not been approved, but has been authorized for emergency use by FDA under an EUA, for the treatment of mild-to-moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death.

The emergency use of PAXLOVID is only authorized for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of drugs and biological products during the COVID-19 pandemic under Section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization revoked sooner.

AUTHORIZED USE

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) for the emergency use of the unapproved product PAXLOVID for the treatment of mild-to-moderate coronavirus disease 2019 (COVID-19) in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death.

LIMITATIONS OF AUTHORIZED USE

- PAXLOVID is not authorized for initiation of treatment in patients requiring hospitalization due to severe or critical COVID-19
- PAXLOVID is not authorized for use as pre-exposure or post-exposure prophylaxis for prevention of COVID-19
- PAXLOVID is not authorized for use for longer than 5 consecutive days

PAXLOVID may be prescribed for an individual patient by physicians, advanced practice registered nurses, and physician assistants that are licensed or authorized under state law to prescribe drugs.

PAXLOVID may also be prescribed for an individual patient by a state-licensed pharmacist under the following conditions:

- Sufficient information is available, such as through access to health records less than 12 months old or consultation with a health care provider in an established provider-patient relationship with the individual patient, to assess renal and hepatic function; and
- Sufficient information is available, such as through access to health records, patient reporting of medical history, or consultation with a health care provider in an established provider-patient relationship with the individual patient, to obtain a comprehensive list of medications (prescribed and non-prescribed) that the patient is taking to assess for potential drug interaction.

The state-licensed pharmacist should refer an individual patient for clinical evaluation (e.g., telehealth, in-person visit) with a physician, advanced practice registered nurse, or physician assistant licensed or authorized under state law to prescribe drugs, if any of the following apply:

- Sufficient information is not available to assess renal and hepatic function.
- Sufficient information is not available to assess for a potential drug interaction.
- Modification of other medications is needed due to a potential drug interaction.
- PAXLOVID is not an appropriate therapeutic option based on the authorized Fact Sheet for Healthcare Providers or due to potential drug interactions for which recommended monitoring would not be feasible.

PAXLOVID is not approved for any use, including for use for the treatment of COVID-19.

PAXLOVID is authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of PAXLOVID under 564(b)(1) of the Food Drug and Cosmetic Act unless the authorization is terminated or revoked sooner.

IMPORTANT SAFETY INFORMATION

PAXLOVID is **contraindicated in patients with a history of clinically significant hypersensitivity reactions** (eg, toxic epidermal necrolysis [TEN] or Stevens-Johnson syndrome) to its active ingredients (nirmatrelvir or ritonavir) or any other components of the product.

Drugs listed in this section are a guide and not considered a comprehensive list of all drugs that may be contraindicated with PAXLOVID. The healthcare provider should consult other appropriate resources such as the prescribing information for the interacting drug for comprehensive information on dosing or monitoring with concomitant use of a strong CYP3A inhibitor such as ritonavir.

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: $Alpha_1$-adrenoreceptor antagonist: alfuzosin; Antianginal: ranolazine; Antiarrhythmic: amiodarone, dronedarone, flecainide, propafenone, quinidine; Anti-gout: colchicine; Antipsychotics: lurasidone, pimozide; Benign prostatic hyperplasia agents: silodosin; Cardiovascular agents: eplerenone, ivabradine; Ergot derivatives: dihydroergotamine, ergotamine, methylergonovine; HMG-CoA reductase inhibitors: lovastatin, simvastatin; Immunosuppressants: voclosporin; Microsomal triglyceride transfer protein inhibitor: lomitapide; Migraine medications: eletriptan, ubrogepant; Mineralocorticoid receptor antagonists: finerenone; Opioid antagonists: naloxegol; PDE5 inhibitor: sildenafil (Revatio®) when used for pulmonary arterial hypertension; Sedative/hypnotics: triazolam, oral midazolam; Serotonin receptor 1A agonist/serotonin receptor 2A antagonist: flibanserin; Vasopressin receptor antagonists: tolvaptan.

Guidance for writing PAXLOVID™ (nirmatrelvir tablets; ritonavir tablets) prescriptions

In addition to specifying the numeric dose of each active ingredient within PAXLOVID, here are some suggestions on details to include*:

Standard Dosing

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Prescription:
2 nirmatrelvir 150-mg tablets (300 mg) and
1 ritonavir 100-mg tablet, taken together, twice daily, with or without food for 5 days.

Please fill prescription by [insert date].

[Additional notes to pharmacy*:]
- Positive SARS-CoV-2 test
- Age ≥18 years OR ≥12 years and weighs ≥40 kg
- Risk factor(s) for progression to severe COVID-19†
- Symptom onset ≤5 days, consistent with mild-to-moderate COVID-19, not requiring hospitalization
- Mild or no known/suspected renal impairment (eGFR ≥60 to <90 mL/min)
- No known or suspected severe hepatic impairment (Child-Pugh Class C)
- No history of significant hypersensitivity reactions
- Concomitant medications (screen for drug interactions)

Moderate Renal Impairment Dosing

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Prescription:
1 nirmatrelvir 150-mg tablet (150 mg) and
1 ritonavir 100-mg tablet, taken together, twice daily, with or without food for 5 days.

Please fill prescription by [insert date].

[Additional notes to pharmacy*:]
- Positive SARS-CoV-2 test
- Age ≥18 years OR ≥12 years and weighs ≥40 kg
- Risk factor(s) for progression to severe COVID-19†
- Symptom onset ≤5 days, consistent with mild-to-moderate COVID-19, not requiring hospitalization
- Patient has moderate renal impairment (eGFR ≥30 to <60 mL/min)
- No known or suspected severe hepatic impairment (Child-Pugh Class C)
- No history of significant hypersensitivity reactions
- Concomitant medications (screen for drug interactions)

Your state, institutional, or local requirements may also require you to write the patient's race/ethnicity, or blood labs for renally impaired patients.

Providers should also specify that completion of the full 5-day treatment course and continued isolation in accordance with public health recommendations are important to maximize viral clearance and minimize transmission of SARS-CoV-2.

Additional prescribing information (also refer to Drug Interactions)

- Prescribe standard dose pack in patients with mild renal impairment (eGFR ≥60 to <90 mL/min)
- PAXLOVID is not recommended in patients with severe renal impairment (eGFR <30 mL/min)
- No dosage adjustment is required when coadministered with other products containing ritonavir or cobicistat
- Patients on ritonavir- or cobicistat-containing HIV or HCV regimens should continue their treatment as indicated

*For additional screening information, consult the **FDA's PAXLOVID Patient Eligibility Screening Checklist Tool for Prescribers**‡ or a similar resource from your local public health authority.

†Consult the **CDC** for the latest information on factors that put patients at high risk for progression to severe COVID-19.‡

‡These links will take you to websites that are owned and operated by the FDA and CDC. Pfizer is not responsible for the content or services of these sites.

IMPORTANT SAFETY INFORMATION (CONT'D)

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:

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

There are limited clinical data available for PAXLOVID. **Serious and unexpected adverse events may occur** that have not been previously reported with PAXLOVID use.

Please see additional Important Safety Information throughout this resource and Fact Sheets for Healthcare Providers and for Patients, Parents, and Caregivers.

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How to distinguish the packaging for standard dosing from moderate renal impairment dosing

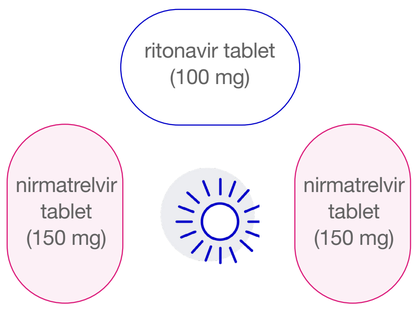
Standard Dose Pack

The blue carton for normal renal function or mild renal impairment has the NDC numbers 0069-1085-30 or 0069-0345-30.

The yellow and blue blister card for **normal renal function** or for **mild renal impairment**. NDCs 0069-0185-06, 0069-0345-06.

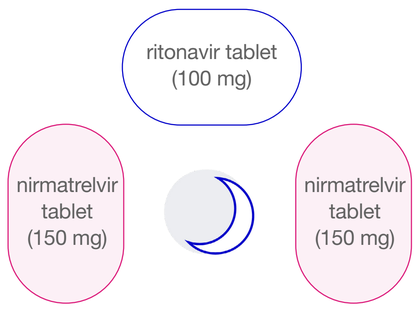
- The standard dosage for PAXLOVID is **300 mg nirmatrelvir (two 150-mg tablets)** with 100 mg ritonavir (one 100-mg tablet), with all three tablets taken together orally, twice daily for 5 days, with or without food.

Morning Dose



Take 3 tablets at the same time.

Evening Dose



Take 3 tablets at the same time.

The blister cards have a bar code for hospital staff to scan.

Moderate Renal Impairment Dose Pack

The yellow carton for **moderate renal impairment** shows the reduced dose in a yellow rectangle with the NDC number 0069-1101-20.*

The white and pink blister card for **moderate renal impairment.** NDC 0069-1101-04.

- For patients with moderate renal impairment, the dosage for PAXLOVID is **150 mg nirmatrelvir (one 150-mg tablet)** with 100 mg ritonavir (one 100-mg tablet), with both tablets taken together orally, twice daily for 5 days, with or without food.

Morning Dose

Take 2 tablets at the same time.

Evening Dose

Take 2 tablets at the same time.

The blister cards have a bar code for hospital staff to scan.

*Renal dosing cartons of PAXLOVID™ may not be available in all areas at this time. Please refer to the **Pharmacist Renal Guide** to understand how to adjust standard dosing cartons for patients with renal impairment.

IMPORTANT SAFETY INFORMATION (CONT'D)

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

Consult Table 1 of the Fact Sheet for Healthcare Providers for clinically significant drug interactions, including contraindicated drugs. Drugs listed in Table 1 are a guide and not considered a comprehensive list of all possible drugs that may interact with PAXLOVID. Consider the potential for drug interactions prior to and during PAXLOVID therapy; review concomitant medications during PAXLOVID therapy and monitor for the adverse reactions associated with the concomitant medications.

Please see additional Important Safety Information throughout this resource and Fact Sheets for Healthcare Providers and for Patients, Parents, and Caregivers.

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Additional Resources

- Additional dosing information at paxlovidhcp.com/dosing
- Answers to questions about drug interactions, high risk factors, and more at paxlovidhcp.com/faq
- FDA's PAXLOVID Screening Eligibility Checklist for Prescribers*
- Pfizer Medical Information's Drug Interaction Checker†
- The Dept. of Health and Human Services (HHS) COVID-19 Therapeutics Locator
- Consult the CDC for the latest information on factors that put patients at high risk for progression to severe COVID-19
- Please refer to the Pharmacist Renal Guide to understand how to adjust standard dosing cartons for patients with renal impairment

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Scan the QR code or click the URL below to download the Fact Sheet for Healthcare Providers.

https://www.paxlovidhcp.com/files/Fact_Sheet_HCP.pdf

Scan the QR code or click the URL below to download the Fact Sheet for Patients, Parents, and Caregivers.

https://www.paxlovidhcp.com/files/Fact_Sheet_Patient.pdf

*These links will take you to websites that are owned and operated by the FDA or HHS. Pfizer is not responsible for the content or services of these sites.
†This drug interaction tool provides information regarding potential drug interactions with the selected product. It is meant to be used as a guide and not considered a comprehensive list of all possible drugs that may interact. The healthcare provider should consult appropriate references for comprehensive information. Please note that information provided by this tool is derived from the product labeling.

IMPORTANT SAFETY INFORMATION (CONT'D)

Hypersensitivity reactions have been reported with PAXLOVID including urticaria, angioedema, dyspnea, mild skin eruptions, and pruritus. Cases of anaphylaxis, TEN, and Stevens-Johnson syndrome have also been reported with ritonavir, a component of PAXLOVID (refer to NORVIR prescribing information). 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**.

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.

Adverse events in the PAXLOVID group (≥1%) that occurred at a greater frequency (≥5 subject difference) than in the placebo group were dysgeusia (6% and <1%, respectively), diarrhea (3% and 2%), hypertension (1% and <1%), and myalgia (1% and <1%). The proportions of subjects who discontinued treatment due to an adverse event were 2% in the PAXLOVID group and 4% in the placebo group.

The following adverse reactions have been identified during post-authorization use of PAXLOVID. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Immune System Disorders: Hypersensitivity reactions
Gastrointestinal Disorders: Abdominal pain, nausea
General Disorders and Administration Site Conditions: Malaise

Required Reporting for Serious Adverse Events and Medication Errors: The prescribing healthcare provider and/or the provider's designee is/are responsible for mandatory reporting of all serious adverse events and medication errors potentially related to PAXLOVID within 7 calendar days from the healthcare provider's awareness of the event.

Please see additional Important Safety Information throughout this resource and Fact Sheets for Healthcare Providers and for Patients, Parents, and Caregivers.

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IMPORTANT SAFETY INFORMATION (CONT'D)

Submit adverse event and medication error reports to FDA MedWatch using one of the following methods:
- **Online:** https://www.fda.gov/medwatch/report.htm
- **Complete and submit a postage-paid** FDA Form 3500 **and returning by mail/fax**
- **Call** 1-800-FDA-1088 **to request a reporting form**

In addition, please provide a copy of all FDA MedWatch forms to: www.pfizersafetyreporting.com, or by fax (1-866-635-8337) or phone (1-800-438-1985).

PAXLOVID is a strong inhibitor of CYP3A and may increase plasma concentrations of drugs that are primarily metabolized by CYP3A. 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. Co-administration with other CYP3A substrates may require a dose adjustment or additional monitoring.

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

Pregnancy: There are no available human data on the use of nirmatrelvir during pregnancy to evaluate for a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Published observational studies on ritonavir use in pregnant women have not identified an increase in the risk of major birth defects. Published studies with ritonavir are insufficient to identify a drug-associated risk of miscarriage. There are maternal and fetal risks associated with untreated COVID-19 in pregnancy.

Lactation: There are no available data on the presence of nirmatrelvir in human or animal milk, the effects on the breastfed infant, or the effects on milk production. A transient decrease in body weight was observed in the nursing offspring of rats administered nirmatrelvir. Limited published data reports that ritonavir is present in human milk. There is no information on the effects of ritonavir on the breastfed infant or the effects of the drug on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for PAXLOVID and any potential adverse effects on the breastfed infant from PAXLOVID or from the underlying maternal condition. Breastfeeding individuals with COVID-19 should follow practices according to clinical guidelines to avoid exposing the infant to COVID-19.

Contraception: Use of ritonavir may reduce the efficacy of combined hormonal contraceptives. Advise patients using combined hormonal contraceptives to use an effective alternative contraceptive method or an additional barrier method of contraception.

Pediatrics: PAXLOVID is not authorized for use in pediatric patients younger than 12 years of age or weighing less than 40 kg. The safety and effectiveness of PAXLOVID have not been established in pediatric patients. The authorized adult dosing regimen is expected to result in comparable serum exposures of nirmatrelvir and ritonavir in patients 12 years of age and older and weighing at least 40 kg as observed in adults, and adults with similar body weight were included in the trial EPIC-HR.

Systemic exposure of nirmatrelvir increases in renally impaired patients with increase in the severity of renal impairment. No dosage adjustment is needed in patients with mild renal impairment. **In patients with moderate renal impairment (eGFR ≥30 to <60 mL/min), reduce the dose of PAXLOVID** to 150 mg nirmatrelvir and 100 mg ritonavir twice daily for 5 days. Prescriptions should specify the numeric dose of each active ingredient within PAXLOVID. Providers should counsel patients about renal dosing instructions. **PAXLOVID is not recommended in patients with severe renal impairment** (eGFR <30 mL/min based on CKD-EPI formula) until more data are available; the appropriate dosage for patients with severe renal impairment has not been determined.

No dosage adjustment of PAXLOVID is needed for patients with either 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 subjects with severe hepatic impairment (Child-Pugh Class C); therefore, **PAXLOVID is not recommended for use in patients with severe hepatic impairment.**

Please see Fact Sheet for Healthcare Providers and Fact Sheet for Patients, Parents, and Caregivers.

Reference: PAXLOVID Fact Sheet for Healthcare Providers. Pfizer Inc.

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