Potentially Significant Drug Interactions, including Contraindicated Drugs

PAXLOVID™ (nirmatrelvir tablets; ritonavir tablets)

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.

Fact Sheet for Healthcare Providers

Fact Sheet for Patients, Parents, and Caregivers

FDA Emergency Use Authorization Letter

Important Information

- Information included in this document relates only to known or suspected effects of interacting medications, and where noted is derived from FDA-approved labeling or from the FDA-authorized fact sheet for PAXLOVID. Pfizer does not suggest or recommend the use of PAXLOVID in any manner other than as described in the EUA Fact Sheet for Healthcare Providers.
- The list of medications is meant to be used as a guide and is not meant to be comprehensive. If a medication is not listed in the EUA Fact Sheet for Healthcare Providers or in this resource, it should not be assumed it is safe to co-administer with PAXLOVID. Please consult the PAXLOVID EUA Fact Sheet for Healthcare Providers and the FDA-approved/authorized labelling for the co-administered medication for information on listed interactions and their treatment-emergent adverse events.
- No clinical advice is given, or implied and healthcare providers must exercise their own judgement in relation to the risks and benefits of combining medications, which depend on factors beyond pharmacokinetic interactions between two medications.
- When considering drug combinations, pharmacokinetic, pharmacodynamics, and safety profile for each medication, in this case PAXLOVID and other medications, this document may be considered to help identify potential sources of interaction. Pfizer has not conducted any studies evaluating the safety and efficacy of PAXLOVID in combination with other medications. Healthcare providers may consider the information below and in the PAXLOVID EUA Fact Sheet for Healthcare Providers in determining if the combination of PAXLOVID with a specific (drug class) / drug is suitable for patient use.
- The information in this document is intended as educational, background information only for healthcare providers prescribing PAXLOVID in accordance with FDA-authorized labeling. If you are a consumer/patient experiencing a medical emergency, call 911 immediately and speak with your healthcare provider. This information should not replace a healthcare provider's medical advice based on clinical judgment or be used in lieu of a COVID-19 consultation when necessary.

Pfizer Medical Affairs

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Drug Class	Clinical Information from FDA's EUA Fact Sheet for PAXLOVID	Clinical Information from FDA-Approved Labeling for Interacting Drug (if available)
Alpha 1-adrenoreceptor Antagonist		
Alfuzosin	**Co-administration contraindicated due to potential hypotension.**	
Analgesics		
Fentanyl	Use Caution. Monitor for respiratory depression and other adverse effects.	
Methadone	Monitor for withdrawal effects and consider dose increase.	
Pethidine (Meperidine)	**Co-administration contraindicated due to potential for serious respiratory depression or hematologic abnormalities.**	
Propoxyphene	**Co-administration contraindicated due to potential for serious respiratory depression or hematologic abnormalities.**	
Antianginal		
Ranolazine	**Co-administration contraindicated due to potential for serious and/or life-threatening reactions.**	
Antiarrhythmics		
Amiodarone	**Co-administration contraindicated due to potential for cardiac arrhythmias.**	
Bepridil	Therapeutic concentration monitoring is recommended if available.	
Dronedarone	**Co-administration contraindicated due to potential for cardiac arrhythmias.**	
Flecainide	**Co-administration contraindicated due to potential for cardiac arrhythmias.**	
Lidocaine (Systemic)	Therapeutic concentration monitoring is recommended if available.	

Drug Class	Clinical Information from FDA's EUA Fact Sheet for PAXLOVID	Clinical Information from FDA-Approved Labeling for Interacting Drug (if available)
Propafenone	Co-administration contraindicated due to potential for cardiac arrhythmias.	
Quinidine	Co-administration contraindicated due to potential for cardiac arrhythmias.	
Anticancer Drugs		
Abemaciclib		Reduce doses of 200 mg twice daily or 150 mg twice daily to 100 mg twice daily. In patients who have had a dose reduction to 100 mg twice daily due to adverse reactions, further reduce dose to 50 mg twice daily. Increase abemaciclib dose after appropriate washout of PAXLOVID.
Apalutamide	Co-administration contraindicated due to potential loss of virologic response and possible resistance.	
Ceritinib	Avoid concomitant use.	If concomitant use is unavoidable, reduce ceritinib dose by approximately one-third, rounded to the nearest multiple of the 150 mg dosage strength. After discontinuation of PAXLOVID, resume ceritinib dose taken prior to initiating PAXLOVID.
Dasatinib	Avoid concomitant use.	If dasatinib must be administered with PAXLOVID, consider a dose decrease to 40 mg daily for patients taking 140 mg daily, 20 mg daily for patients taking 100 mg daily, and 20 mg daily for patients taking 70 mg daily. For patients taking 60 mg or 40 mg daily, consider interrupting dasatinib until the inhibitor is discontinued. Allow a washout period of approximately 1 week after the inhibitor is stopped before reinitiating dasatinib.
Encorafenib	Avoid co-administration due to potential risk of serious adverse effects such as QT interval prolongation.	
Ibrutinib	Avoid use.	
Ivosidenib	Avoid co-administration due to potential risk of serious adverse effects such as QT interval prolongation.	
Neratinib	Avoid use.	
Nilotinib	Avoid concomitant use.	Should treatment with nitrmatrelvir; ritonavir be required, hold nilotinib. If coadministered, reduce dosage to 300 mg once daily in patients with resistant or intolerant Ph+ CML or to 200 mg once daily in patients with newly diagnosed Ph+ CML-CP. Monitor closely for prolongation of the QT interval.
Venetoclax	Avoid use.	
Vinblastine	Monitor for hematologic or gastrointestinal side effects.	
Vincristine	Monitor for hematologic or gastrointestinal side effects.	

Drug Class	Clinical Information from FDA's EUA Fact Sheet for PAXLOVID	Clinical Information from FDA-Approved Labeling for Interacting Drug (if available)
Anticoagulants		
Rivaroxaban	Avoid concomitant use.	
Warfarin	Closely monitor INR if co-administration is necessary.	
Dabigatran	Increased bleeding risk with dabigatran. Depending on dabigatran indication and renal function, reduce dose of dabigatran or avoid concomitant use. Refer to the dabigatran product label for further information.	
Anticonvulsants		
Carbamazepine	**Co-administration contraindicated due to potential loss of virologic response and possible resistance.**	
Phenobarbital	**Co-administration contraindicated due to potential loss of virologic response and possible resistance.**	
Phenytoin	**Co-administration contraindicated due to potential loss of virologic response and possible resistance.**	
Antidepressants		
Bupropion	Monitor for an adequate clinical response to bupropion due to decreased concentrations.	
Trazodone	A lower dose of trazodone should be considered. Refer to trazadone product label for further information.	
Antifungals		
Ketoconazole	Use with caution. Monitor for adverse effects.	
Isavuconazonium Sulfate	**Co-administration contraindicated due to increased concentrations of isavuconazole.**	
Itraconazole		Use with caution.
Voriconazole	Avoid concomitant use.	
Anti-Gout		
Colchicine	**Co-administration contraindicated due to potential for serious and/or life-threatening reactions in patients with renal and/or hepatic impairment.**	
Anti-HIV		
Bictegravir/Emtricitabine/Tenofovir		No dose adjustment needed. May significantly increase concentrations of bictegravir and tenofovir. Monitor for adverse effects.
Delavirdine		No dose adjustment needed. May increase concentrations of PAXLOVID. Monitor for adverse effects.
Didanosine		No dose adjustment needed.
Efavirenz		No dose adjustment needed. Consider monitoring for liver enzymes.

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Maraviroc		Reduce dose of maraviroc in adults to 150 mg twice daily.
Nevirapine		No dose adjustment needed.
Raltegravir		No dose adjustment needed.
Zidovudine		No dose adjustment needed.
Anti-HIV Protease Inhibitors		
Amprenavir	Patients on ritonavir- or cobicistat-containing HIV regimens should continue their treatment as indicated. Monitor for adverse effects.	No dose modification.
Atazanavir	Patients on ritonavir- or cobicistat-containing HIV regimens should continue their treatment as indicated. Monitor for adverse effects.	No dose modification.
Darunavir	Patients on ritonavir- or cobicistat-containing HIV regimens should continue their treatment as indicated. Monitor for adverse effects.	No dose modification.
Fosamprenavir	Patients on ritonavir- or cobicistat-containing HIV regimens should continue their treatment as indicated. Monitor for adverse effects.	No dose modification.
Indinavir	Patients on ritonavir- or cobicistat-containing HIV regimens should continue their treatment as indicated. Monitor for adverse effects.	No dose modification.
Nelfinavir	Patients on ritonavir- or cobicistat-containing HIV regimens should continue their treatment as indicated. Monitor for adverse effects.	No dose modification.
Saquinavir	Patients on ritonavir- or cobicistat-containing HIV regimens should continue their treatment as indicated. Monitor for adverse effects.	No dose modification.
Tipranavir	Patients on ritonavir- or cobicistat-containing HIV regimens should continue their treatment as indicated. Monitor for adverse effects.	No dose modification.
Anti-Infectives		
Bedaquiline		Avoid use unless benefits outweigh risks. Monitor ECGs.

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Clarithromycin		Clarithromycin may be administered without dosage adjustment to patients with normal renal function taking ritonavir. For patients with CL_{CR} 30 to 60 mL/min, the dose of clarithromycin should be reduced by 50%. For patients with CL_{CR} < 30 mL/min, the dose of clarithromycin should be decreased by 75%.
Erythromycin		Increased erythromycin levels. Monitor ECG for QT prolongation.
Rifabutin		Reduce dose of rifabutin by at least 75%. Monitor for adverse effects.
Rifampin	**Co-administration contraindicated due to potential loss of virologic response and possible resistance. Alternate antimycobacterial drugs such as rifabutin should be considered.**	
Antipsychotics		
Lurasidone	**Co-administration contraindicated due to serious and/or life-threatening reactions such as cardiac arrhythmias.**	
Pimozide	**Co-administration contraindicated due to serious and/or life-threatening reactions such as cardiac arrhythmias.**	
Clozapine	**Co-administration contraindicated due to serious and/or life-threatening reactions such as cardiac arrhythmias.**	
Quetiapine	Reduce dose and monitor for adverse effects. Refer to the quetiapine prescribing information for recommendations.	Caution is indicated when quetiapine is administered with inhibitors of cytochrome P450 3A.
Calcium Channel Blockers		
Amlodipine	Use with caution. Consider decreasing the dose and monitor for adverse effects.	
Diltiazem	Use with caution. Consider decreasing the dose and monitor for adverse effects.	
Felodipine	Use with caution. Consider decreasing the dose and monitor for adverse effects.	
Nicardipine	Use with caution. Consider decreasing the dose and monitor for adverse effects.	
Nifedipine	Use with caution. Consider decreasing the dose and monitor for adverse effects.	
Cardiac Glycoside		
Digoxin	Use with caution and monitor serum digoxin levels.	
Endothelin Receptor Antagonists		
Bosentan	Discontinue use at least 36 hours prior to initiation of PAXLOVID.	

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Ergot Derivatives		
Dihydroergotamine	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.	
Ergotamine	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.	
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.	
Hepatitis C Direct Acting Antivirals		
Elbasvir/Grazoprevir	Use with caution and monitor ALT levels. Consider decreasing dose or consulting with Infectious disease specialist.	
Glecaprevir/Pibrentasvir	Avoid use with PAXLOVID. Consider another regimen.	
Ombitasvir/Paritaprevir/Ritonavir and Dasabuvir	Patients on ritonavir-containing HCV regimens should continue their treatment as indicated. Monitor for adverse effects.	No dose modification
Ritonavir-Containing HCV regimens	Continue treatment as indicated. No dose adjustment needed. Monitor for adverse effects.	
Sofosbuvir/Velpatasvir/Voxilaprevir		Plasma concentration of Velpatasvir and/or Voxilaprevir may increase.
Herbal Products		
St. John's Wort (*hypericum perforatum*)	Co-administration contraindicated due to potential loss of virologic response and possible resistance.	
HMG-CoA Reductase Inhibitors		
Atorvastatin	Consider temporary discontinuation of atorvastatin during treatment with PAXLOVID. Atorvastatin does not need to be held prior to or after completing PAXLOVID.	
Lovastatin	Co-administration contraindicated due to potential for myopathy including rhabdomyolysis. Discontinue use of lovastatin at least 12 hours prior to initiation of PAXLOVID, during the 5 days of PAXLOVID treatment and for 5 days after completing PAXLOVID.	

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Rosuvastatin	Consider temporary discontinuation of rosuvastatin during treatment with PAXLOVID. Rosuvastatin does not need to be held prior to or after completing PAXLOVID.	
Simvastatin	**Co-administration contraindicated due to potential for myopathy including rhabdomyolysis.** **Discontinue use of simvastatin at least 12 hours prior to initiation of PAXLOVID, during the 5 days of PAXLOVID treatment and for 5 days after completing PAXLOVID.**	
Hormonal Contraception		
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		
Cyclosporine	Monitor therapeutic concentration.	Use with caution.
Sirolimus	Avoid concomitant use.	If co-administered, monitor sirolimus concentrations.
Tacrolimus		Reduce dose of tacrolimus. Monitor tacrolimus concentrations and tacrolimus-associated adverse reactions.
Long-Acting Beta-adrenoceptor Agonist		
Salmeterol	Co-administration not recommended due to increased risk of cardiovascular adverse events.	
PDE5 Inhibitors		
Sildenafil (Revatio) for Pulmonary Arterial Hypertension	**Co-administration contraindicated due to the potential for sildenafil associated adverse events, including visual abnormalities hypotension, prolonged erection, and syncope.**	
Sedatives/Hypnotics		
Midazolam (oral)	**Co-administration contraindicated due to potential for extreme sedation and respiratory depression.**	
Midazolam (parenterally)	Administer in clinical setting to monitor for adverse effects. Reduce dose of midazolam (parenterally) if more than one dose is needed.	
Triazolam	**Co-administration contraindicated due to potential for extreme sedation and respiratory depression.**	

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Systemic Corticosteroids		
Betamethasone	Monitor for adverse effects. Consider switching to beclomethasone or prednisolone.	
Budesonide	Monitor for adverse effects. Consider switching to beclomethasone or prednisolone.	
Ciclesonide	Monitor for adverse effects. Consider switching to beclomethasone or prednisolone.	
Dexamethasone	Monitor for adverse effects. Consider switching to beclomethasone or prednisolone.	
Fluticasone	Monitor for adverse effects. Consider switching to beclomethasone or prednisolone.	
Methylprednisolone	Monitor for adverse effects. Consider switching to beclomethasone or prednisolone.	
Mometasone	Monitor for adverse effects. Consider switching to beclomethasone or prednisolone.	
Prednisone	Monitor for adverse effects. Consider switching to beclomethasone or prednisolone.	
Triamcinolone	Monitor for adverse effects. Consider switching to beclomethasone or prednisolone.	

Additional Information

- For any questions, contact Pfizer US Medical Information by visiting www.pfizermedinfo.com or calling 1-800-438-1985.
- As a result of ongoing research, this information may change from time to time based on new information. Pfizer has made all attempts to ensure the accuracy of this information based on relevant data in the public domain.
- If this document was obtained from a source other than Pfizer's Medical website (https://pfizermedical.pfizerpro.com), please visit the webpage for the most up-to-date version.
- All FDA-approved labeling for interacting drugs referenced in this resource were accessed on **3/20/2022**.