

## MANAGEMENT OF PAXLOVID DRUG-DRUG-INTERACTIONS

This list is not meant to be all inclusive. Drug-drug interactions can be checked more completely at <u>Liverpool COVID-19</u> <u>Drug-Drug Interaction website</u>. Additional resources include <u>NIH</u> recommendations for drug-drug interactions between PAXLOVID and <u>UpToDate</u> PAXLOVID drug information.

\*\*Tip: If you use CONTROL + F, you can type the name of the drug you are looking to find on the list.

Drug class	Recommendation (inhibition resolves approximately 3 days after PAXLOVID is discontinued. Unless otherwise stated, <b>hold</b> means a medication should be stopped for <b>8 days</b> from the first dose of PAXLOVID. <b>Very sensitive or narrow therapeutic index CYP3A4 drugs</b> may need to be restarted <b>10 days</b> after the first dose of PAXLOVID)
Antibiotics	
Rifampin	Do not use PAXLOVID, consider an alternative COVID-19 therapy
Rifapentine	Do not use PAXLOVID, consider an alternative COVID-19 therapy
Clarithromycin	Co-administration with nirmatrelvir/ritonavir has not been studied but may increase Clarithromycin concentrations, Clarithromycin doses greater than 1 g per day should not be coadministered with ritonavir dosed as a pharmacokinetic enhancer.
Erythromycin	Co-administration has not been studied, but may increase Erythromycin concentrations. Use with caution as erythromycin has a known risk of QT prolongation.
Alpha-1 blockers	
Alfuzosin	Do not use PALOVID, consider an alternative COVID-19 therapy or hold alfuzosin if appropriate (alfuzosin treatment would have to be resumed 3 days after the last dose of PAXLOVID)
Silodosin	Do not use PAXLOVID, consider an alternative COVID-19 therapy or hold solodosin if appropriate
Tamsulosin	Do not use PAXLOVID, consider an alternative COVID-19 therapy or hold tamsulosin if appropriate
Analgesics	
Piroxicam	Hold Piroxicam doses
Anti-arrhythmic (other than sotalol)	
Amiodarone	Do not use PAXLOVID, consider an alternative COVID-19 therapy
Disopyramide	Do not use PAXLOVID, consider an alternative COVID-19 therapy
Dofetilide	Do not use PAXLOVID, consider an alternative COVID-19 therapy
Dronedarone	Do not use PAXLOVID, consider an alternative COVID-19 therapy
Flecainide	Do not use PAXLOVID, consider an alternative COVID-19 therapy
Lidocaine (systemic)	Use with caution. Therapeutic monitoring is recommended if available
Mexiletine	Do not use PAXLOVID, consider an alternative COVID-19 therapy
Propafenone	Do not use PAXLOVID, consider an alternative COVID-19 therapy
Quinidine	Do not use PAXLOVID, consider an alternative COVID-19 therapy
Anticancer Medications	
	Do not use PAXLOVID, consider an alternative COVID-19 therapy

Abemaciclib	Do not use PAXLOVID, consider an alternative COVID-19 therapy
Ceritinib	Do not use PAXLOVID, consider an alternative COVID-19 therapy. If necessary to use consult with pharmacist about dose reduction.
Dasatinib	Do not use PAXLOVID, consider an alternative COVID-19 therapy
Encorafenib	Do not use PAXLOVID, consider an alternative COVID-19 therapy. If necessary to use consult with pharmacist about dose reduction.
Ibrutinib	Do not use PAXLOVID, consider an alternative COVID-19 therapy
Ivosidenib	Do not use PAXLOVID, consider an alternative COVID-19 therapy
Neratinib	Do not use PAXLOVID, consider an alternative COVID-19 therapy
Palbociclib	Do not use PAXLOVID, consider an alternative COVID-19 therapy. If necessary to use consult with pharmacist about dose reduction.
Venetoclax	Do not use PAXLOVID, consider an alternative COVID-19 therapy
Vinblastine	Consult with oncologist or pharmacist. Would need assessment prior to resuming therapy.
Vincristine	Consult with oncologist or pharmacist. Would need assessment prior to resuming therapy.
Anticoagulants	
Apixaban	2.5 mg BID dose <b>may be</b> considered. Potential risk of increased bleeding, decision to continue Apixaban should be based on a risk benefit discussion.
Dabigatran	Potential risk of increased bleeding, decision to continue Dabigatran should be made based on a risk benefit discussion. If Dabigatran is continued, take together with PAXLOVID.
Edoxaban	Reduced edoxaban dose to 30 mg daily <b>may be</b> considered. Potential risk of increased bleeding, decision to continue Edoxaban should be based on a risk benefit discussion.
Rivaroxaban	Do not use PAXLOVID, consider an alternative COVID-19 therapy
Warfarin	Carefully monitor INR. Increased risk of both super and supratherapeutic INR on usual dose.
Anti-epileptics	
Carbamazepine	Do not use PAXLOVID, consider an alternative COVID-19 therapy
Phenobarbital	Do not use PAXLOVID, consider an alternative COVID-19 therapy
Phenytoin	Do not use PAXLOVID, consider an alternative COVID-19 therapy
Primidone	Do not use PAXLOVID, consider an alternative COVID-19 therapy
Antifungals	
ltraconazole	Use caution due to potential for increased itraconazole concentrations. Do not use high doses of itraconazole (>200 mg/day). Monitor for gastrointestinal and hepatic adverse effects.
Ketoconazole	Use caution and consider dose decrease of ketoconazole due to potential for increased ketoconazole concentrations. Do not use high doses of ketoconazole (>200 mg/day). Monitor for gastrointestinal and hepatic adverse reactions

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Voriconazole	Do not use PAXLOVID, consider an alternative COVID-19 therapy
Isavuconazonium	Do not use PAXLOVID, consider an alternative COVID-19 therapy
Antipsychotics	
Aripiprazole	Co-administration has not been studied. PAXLOVID could potentially increase aripiprazole concentrations. Monitor adverse effects and decrease aripiprazole dosage if needed.
Brexpiprazole	Consider therapy modification, could reduce brexpiprazole dose by 50%, monitor for adverse effects
Clozapine	Do not use PAXLOVID, consider an alternative COVID-19 therapy
Lumateperone	Do not use PAXLOVID, consider an alternative COVID-19 therapy
Lurasidone	Do not use PAXLOVID, consider an alternative COVID-19 therapy
Pimavanserin	Consider therapy modification, could reduce pimavanserin dose to 10mg daily
Pimozide	Do not use PAXLOVID, consider an alternative COVID-19 therapy
Quetiapine	Co-administration has not been studied but not recommended. If co-administration is necessary, reduce quetiapine dose and monitor for quetiapine-associated adverse reactions.
Antiretrovirals	
HIV medications	No dose adjustments necessary (even if on ritonavir/cobicistat-boosted regimen) – monitor for protease inhibitor adverse effects – see IDSA/ HIVMA brief
Benzodiazepines	
Alprazolam	Reduce alprazolam dose by 50%, hold Alprazolam doses, or consider changing to lorazepam temporarily
Clonazepam	Do not use PAXLOVID. Consider changing to lorazepam temporarily or hold Clonazepam doses.
Diazepam	Do not use PAXLOVID. Consider changing to lorazepam temporarily or hold Diazepam doses.
Lorazepam	Use a typical recommended dose or equivalent dose if switching from another benzodiazepine temporarily.
Midazolam (oral)	Do not use with PAXLOVID. Consider changing to lorazepam temporarily or hold Midazolam doses.
Triazolam	Do not use with PAXLOVID. Consider changing to lorazepam temporarily or hold Triazolam doses.

Calcineurin inhibitors	
Cyclosporine	Preferentially administer an alternative. Patients <b>within 3 months</b> of transplant should not receive Paxlovid. If outside of that 3-month window, and Paxlovid is started, refer back to transplant provider or pharmacist for monitoring and possible dose adjustment.
Tacrolimus	Preferentially administer an alternative. Patients <b>within 3 months</b> of transplant should not receive Paxlovid. If outside of that 3-month window, and Paxlovid is started, refer back to transplant provider or pharmacist for monitoring and possible dose adjustment.

Calcium Channel Blockers	
Amlodipine	Use with caution, monitoring is recommended, could consider a dose decrease
Diltiazem	Use with caution, monitoring is recommended, could consider a dose decrease
Felodipine	Use with caution, monitoring is recommended, could consider a dose decrease
Nicardipine	Use with caution, monitoring is recommended, could consider a dose decrease
Nifedipine	Use with caution, monitoring is recommended, could consider a dose decrease
Verapamil	Use with caution, monitoring is recommended, could consider a dose decrease
Cystic Fibrosis (CF)TR Modulators	
Elexacaftor/tezacaftor/ivacaftor (Trikafta)	Day 1 – 2 orange tablets in morning only Days 2 – 4 – No Trikafta Day 5 (last day of PAXLOVID) - 2 orange tablets in morning only Days 6 – 8 – No Trikafta Day 9 -resume normal Trikafta dosing Contact Cystic Fibrosis (CF) team for case by case management
Ivacaftor (Kalydeco)	Day 1- 1 tablet in the morning only Days 2 – 4 – No ivacaftor Day 5(last day of PAXLOVID) – 1 tablet in the morning only Days 6 – 8 – No ivacaftor Day 9 - resume normal ivacaftor dosing Contact Cystic Fibrosis (CF) team for case by case management
Tezacaftor/ivacaftor (Symdeko)	Day 1 – 1 yellow tablet in the morning only Days 2 – 4 – No Symdeko Day 5 (last day of PAXLOVID) - 1 yellow tablet in the morning only Days 6 – 8 – No Symdeko Day 9 – resume normal Symdeko dosing Contact Cystic Fibrosis (CF) team for case by case management
Lumecaftor/ivacaftor (Orkambi)	Do not use PAXLOVID, consider alternative COVID-19 therapy. Contact Cystic Fibrosis (CF) team for case by case management
CGRP Antagonist	
Ubrogepant	Do not use PAXLOVID, consider alternative COVID-19 treatment
Rimagepant	Do not use PAXLOVID, consider alternative COVID-19 treatment
Chemotherapy (oral or parenteral or small molecule)	Contact oncology pharmacist team
Ergot alkaloids	
Dihydroergotamine	Do not use PAXLOVID, consider an alternative COVID-19 treatment
Ergoloid mesylates	Do not use PAXLOVID, consider an alternative COVID-19 treatment
Ergonovine	Do not use PAXLOVID, consider an alternative COVID-19 treatment
Ergotamine	Do not use PAXLOVID, consider an alternative COVID-19 treatment
Methylergonovine	Do not use PAXLOVID, consider an alternative COVID-19 treatment

Corticosteroids	
Beclomethasone	No specific action needed; monitor for adverse events

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Betamethasone	Increased risk for Cushing's syndrome and adrenal suppression. Alternative corticosteroids including beclomethasone and prednisolone should be considered.
Budesonide	Increased risk for Cushing's syndrome and adrenal suppression. Alternative corticosteroids including beclomethasone and prednisolone should be considered.
Ciclesonide	Increased risk for Cushing's syndrome and adrenal suppression. Alternative corticosteroids including beclomethasone and prednisolone should be considered.
Dexamethasone	Increased risk for Cushing's syndrome and adrenal suppression. Alternative corticosteroids including beclomethasone and prednisolone should be considered.
Fluticasone	Increased risk for Cushing's syndrome and adrenal suppression. Alternative corticosteroids including beclomethasone and prednisolone should be considered.
Mometasone	Increased risk for Cushing's syndrome and adrenal suppression. Alternative corticosteroids including beclomethasone and prednisolone should be considered.
Methylprednisolone	Increased risk for Cushing's syndrome and adrenal suppression. Alternative corticosteroids including beclomethasone and prednisolone should be considered.
Prednisone	Increased risk for Cushing's syndrome and adrenal suppression. Alternative corticosteroids including beclomethasone and prednisolone should be considered.
Triamcinolone	Increased risk for Cushing's syndrome and adrenal suppression. Alternative corticosteroids including beclomethasone and prednisolone should be considered.
mTOR inhibitors	
Everolimus	Preferentially administer an alternative Patients <b>within 3 months</b> of transplant should not receive Paxlovid.
	If outside of that 3-month window, and Paxlovid is started, refer back to transplant provider or pharmacist for monitoring and possible dose adjustment.
Sirolimus	Preferentially administer an alternative Patients <b>within 3 months</b> of transplant should not receive Paxlovid.
	If outside of that 3-month window, and Paxlovid is started, refer back to transplant provider or pharmacist for monitoring and possible dose adjustment.
Opioids	
Codeine	May increase concentrations of codeine. Reduce codeine dose by 50% while on PAXLOVID, monitor carefully for signs of opioid overdose
Fentanyl	Do not use PAXLOVID, consider alternative COVID-19 therapy or hold medication if appropriate
Hydrocodone	May increase concentrations of hydrocodone. Reduce hydrocodone dose by 50% while on PAXLOVID, monitor carefully for signs of opioid overdose
Meperidine	Do not use PAXLOVID, consider alternative COVID-19 therapy or hold medication if appropriate
Methadone	Do not use PAXLOVID, consider alternative COVID-19 therapy or hold medication if appropriate
Morphine	May increase concentrations of morphine. Reduce morphine dose by 50% while on PAXLOVID, monitor carefully for signs of opioid overdose. If on a controlled release medication will need a new prescription for lower dose.

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Outroodere	May increase concentrations of evycodene. Deduce evycedene dece by 75%
Oxycodone	May increase concentrations of oxycodone. Reduce oxycodone dose by 75%, monitor carefully for signs of opioid overdose. If on a controlled release medication will need a new prescription for lower dose.
Potassium-sparing diuretics	
Eplerenone	Do not use PAXLOVID, consider alternative COVID-19 therapy or hold medication if appropriate
Finerenone	Do not use PAXLOVID, consider alternative COVID-19 therapy or hold medication if appropriate
P2Y12 antagonists	
Clopidogrel	Potential for reduced effect of clopidogrel. Avoid PAXLOVID, consider an alternative COVID-19 treatment or transition to prasugrel in patients at high risk of thrombosis.
Ticagrelor	Do not use PAXLOVID, consider an alternative COVID-19 treatment or consider transitioning to prasugrel
Prasugrel	Decision to continue prasugrel should be based on risk benefit decision.
PDE5 inhibitors	
Avanafil	Hold avanafil
Sildenafil	Erectile dysfunction, Raynaud phenomenon: hold sildenafil Pulmonary hypertension, pulmonary edema: do not use PAXLOVID, consider an alternative COVID-19 treatment
Tadalafil	BPH, erectile dysfunction, Raynaud phenomenon: hold tadalafil Pulmonary hypertension: do not use PAXLOVID, consider an alternative COVID-19 treatment
Vardenafil	Erectile dysfunction, Raynaud phenomenon: hold vardenafil Pulmonary hypertension: do not use PAXLOVID, consider an alternative COVID-19 treatment
Statins	
Atorvastatin	Hold atorvastatin
Lovastatin	Hold lovastatin, discontinue at least 12 hours prior to PAXLOVID
Rosuvastatin	Hold rosuvastatin
Simvastatin	Hold simvastatin, discontinue at least 12 hours prior to PAXLOVID
Triptans	
Eletriptan	Hold eletriptan
Zolmitriptan	Hold zolmitriptan
Miscellaneous	
Apalutamide	Do not use PAXLOVID, consider an alternative COVID-19 treatment
Bosentan	Do not use PAXLOVID, consider an alternative COVID-19 treatment or discontinue use of bosentan at least 36 hours prior to starting PAXLOVID
Bupropion	PAXLOVID can decrease the efficacy of Bupropion, monitor for an adequate clinical response to bupropion.
Buspirone	Reduce buspirone dose by 50%
Cilostazol	Consider therapy modification, could reduce cilostazol dose to 50mg twice daily

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Colchicine	Use with caution due to risk of increased colchicine concentrations, consider dose reduction or holding colchicine. Do not use PAXLOVID, consider an alternative COVID-19 treatment with colchicine in those with renal or hepatic impairment.
Digoxin	Use with caution due to risk of increased digoxin concentrations. Reduce the digoxin dose by approximately 30 - 50% or reduce the dosing frequency. Therapeutic monitoring of serum digoxin levels is recommended.
Domperidone	Hold domperidone
Estradiol	OCP - could fail, use back-up contraceptive. HRT – could have menopausal symptoms
Flibanserin	Do not use PAXLOVID, consider an alternative COVID-19 treatment
Glecaprevir and pibrentasvir	Do not use PAXLOVID, consider an alternative COVID-19 treatment
Ivabradine	Do not use PAXLOVID, consider an alternative COVID-19 treatment
Lonafarnib	Do not use PAXLOVID, consider an alternative COVID-19 treatment
Lomitapide	Hold Lomitapide doses
Naloxegol	Hold naloxegol
Ranolazine	Do not use PAXLOVID, consider an alternative COVID-19 treatment.
Saxagliptin	Reduce saxagliptin 2.5mg daily; hold saxagliptin or saxagliptin-containing combination product if unable
Salmeterol	Hold salmeterol Use alternative beta-2-agonist if unable to hold salmeterol
St. John's Wort	Do not use PAXLOVID, consider alternative COVID-19 treatment or hold St. John's Wort
Suvorexant	Hold suvorexant
Tolvaptan	Do not use PAXLOVID or hold tolvaptan
Trazodone	Reduce trazodone by 50% due to increased risk of trazodone concentrations and monitor for increased trazodone effects (sedation, QTc prolongation)
Ubrogepant	Do not use PAXLOVID, consider an alternative COVID-19 treatment or hold ubrogepant
Vilazodone	Do not use PAXLOVID, consider an alternative COVID-19 treatment
Voclosporin	Do not use PAXLOVID, consider an alternative COVID-19 treatment
Vorapaxar	Do not use PAXLOVID, consider an alternative COVID-19 treatment