MICHIGAN MEDICINE
UNIVERSITY OF MICHIGAN

MANAGEMENT OF PAXLOVID DRUG-DRUG-INTERACTIONS

This list is not meant to be all inclusive. Drug-drug interactions can be checked more completely at Liverpool COVID-19 Drug-Drug Interaction website. Please view **Appendix B** to identify preferred pharmacist to contact for questions.

Drug class	[1]Recommendation (inhibition resolves approximately 3 days after Paxlovid is discontinued. Unless otherwise stated, interacting medications should be managed (held/dose reduced/extra monitoring) for **8 days** from the first dose of Paxlovid. **Very sensitive or narrow therapeutic index CYP3A4 drugs** may need to be restarted **10 days** after the first dose of Paxlovid)
Antibiotics	
Clarithromycin	Contact infectious diseases PharmD for case-by-case management based on indication
Erythromycin	Hold erythromycin[1]
Rifampin	Do not use Paxlovid
Rifapentine	Do not use Paxlovid
Alpha-1 blockers	
Alfuzosin	Hold alfuzosin[1]
Silodosin	Hold silodosin[1]
Tamsulosin	Hold tamsulosin[1]
Anti-arrhythmic (other than sotalol)	
Amiodarone	Do not use Paxlovid
Disopyramide	Do not use Paxlovid
Dofetilide	Do not use Paxlovid
Dronaderone	Do not use Paxlovid
Flecainide	Do not use Paxlovid
Mexilitine	Do not use Paxlovid
Propafenone	Do not use Paxlovid
Quinidine	Do not use Paxlovid
Anti-epileptics	
Carbamazepine	Do not use Paxlovid
Phenobarbital	Do not use Paxlovid
Phenytoin	Do not use Paxlovid
Primidone	Do not use Paxlovid
Antipsychotics	
Aripiprazole	Reduce aripiprazole dose 50%, monitor for sedation, restlessness, dizziness, confusion[1]
Brexpiprazole	Reduce brexpiprazole dose 50%, monitor for sedation, restlessness, dizziness, confusion[1]
Cariprazine	Contact psychiatry PharmD for case-by-case management based on indication
Clozapine	Do not use Paxlovid
Iloperidone	Contact psychiatry PharmD for case-by-case management based on indication
Lumateperone	Do not use Paxlovid
Lurasidone	Contact psychiatry PharmD for case-by-case management based on indication
Pimavenserin	Reduce pimavenserin dose to 10 mg daily or hold if unable[1]
Pimozide	Do not use Paxlovid
Quetiapine	Contact psychiatry PharmD for case-by-case management based on indication
Antiretrovirals	
HIV medications	For maraviroc, contact Infectious Diseases PharmD for case-by-case management. For other 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%[1]
Chlordiazepoxide	Use with caution[1]
Clobazam	Use with caution[1]
Clonazepam	Use with caution[1]
Clorazepate	Hold clorazepate UNLESS used for seizures[1] If used for seizure management, do not use Paxlovid
Diazepam	Use with caution[1]
Estazolam	Hold estazolam[1]
Flurazepam	Hold flurazepam[1]
Midazolam (oral)	Do not use midazolam oral
Triazolam	Do not use triazolam
Calcineurin inhibitors	
Cyclosporine	Preferentially administer sotrovimab. See **Appendix A** below for management recommendations.
Tacrolimus	Preferentially administer sotrovimab. See **Appendix A** below for management recommendations.
Calcium Channel Blockers	
Amlodipine	Reduce dose by 50%[1]
Diltiazem	Use with caution[1]
Felodipine	Use with caution[1]
Nicardipine	Use with caution[1]
Nifedipine	Use with caution[1]
Verapamil	Use with caution[1]
CFTR 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
Ivacaftor (Kalydeco)	Day 1: 1 tablet in the morning only Days 2 – 4: No ivacaftor Day 4: 1 tablet in the morning only Days 6 – 8: No ivacaftor Day 9: resume normal ivacaftor dosing
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
Lumecaftor/ivacaftor (Orkambi)	Do not use Paxlovid
CGRP Antagonist	
Ubrogepant	Hold ubrogepant[1]
Rimegepant	Hold rimegepant[1]
Corticosteroids (oral)	Standing corticosteroid: Consider reducing corticosteroid dose by 50-75% after weighing risk/benefit of short-term increase in steroid exposure Do NOT use oral corticosteroid for mild/moderate COVID-19 without hypoxia

Direct oral anticoagulants	
Apixaban	Doses >2.5 mg BID: reduce apixaban dose by 50%[1] Dose = 2.5 mg BID: Contact cardiology PharmD for case-by-case management based on indication
Dabigatran	Can co-administer with Paxlovid
Edoxaban	Reduce edoxaban dose to 30 mg daily[1]
Rivaroxaban	Do not use Paxlovid
Ergot alkaloids	
Dihydroergotamine	Do not use Paxlovid
Ergoloid mesylates	Do not use Paxlovid
Ergonovine	Do not use Paxlovid
Ergotamine	Do not use Paxlovid
Methylergonovine	Do not use Paxlovid
Inhaled corticosteroids	
Beclomethasone	No specific action needed; monitor for adverse events[1]
Budesonide	May lead to systemic corticosteroid exposure. Hold if possible or monitor for adverse events[1]
Ciclesonide	No specific action needed; monitor for adverse events[1]
Fluticasone	May lead to systemic corticosteroid exposure. Hold if possible or monitor for adverse events[1]
Mometasone	May lead to systemic corticosteroid exposure. Hold if possible or monitor for adverse events[1]
mTOR inhibitors	
Everolimus	Oncology: Preferentially administer sotrovimab. See **Appendix A** below for management recommendations. Solid organ or hematopoietic cell transplant: Preferentially administer sotrovimab. See **Appendix A** below for management recommendations.
Sirolimus	Solid organ or hematopoietic cell transplant: Preferentially administer sotrovimab. See **Appendix A** below for management recommendations.
Opioids	
Codeine	Use codeine with caution, monitor carefully for signs of opioid overdose[1]
Fentanyl	Reduce fentanyl dose by 50% while on Paxlovid, monitor carefully for signs of opioid overdose[1]
Hydrocodone	New start / PRN: consider reducing starting hydrocodone dose by 50%, monitor carefully[1] Chronic maintenance: reduce hydrocodone dose by 50%, monitor carefully for signs of opioid overdose[1]
Meperidine	Use with caution[1]
Oxycodone	Reduce oxycodone dose by 75%, monitor carefully for signs of opioid overdose[1]
Tramadol	Monitor carefully for signs of tramadol toxicity[1]
Potassium-sparing diuretics	
Eplerenone	Do not use Paxlovid
Finerenone	Hold finerenone[1]

P2Y12 antagonists	
Clopidogrel	Contact cardiology PharmD for case-by-case management based on indication and timing of stent placement
Ticagrelor	Contact cardiology PharmD for case-by-case management based on indication and timing of stent placement
Prasugrel	Can co-administer with Paxlovid
PDE5 inhibitors	
Avanafil	Hold avanafil[1]
Sildenafil	Erectile dysfunction, Raynaud phenomenon: hold sildenafil[1] Pulmonary hypertension, pulmonary edema: do not use Paxlovid
Tadalafil	BPH, erectile dysfunction, Raynaud phenomenon: hold tadalafil[1] Pulmonary hypertension: do not use Paxlovid
Vardenafil	Erectile dysfunction, Raynaud phenomenon: hold vardenafil[1] Pulmonary hypertension: do not use Paxlovid
Statins	
Atorvastatin	Hold atorvastatin[1]
Lovastatin	Hold lovastatin[1]
Rosuvastatin	Hold rosuvastatin[1]
Simvastatin	Hold simvastatin[1]
Triptans	
Eletriptan	Hold eletriptran[1]
Oral chemotherapy / small molecules	Contact oncology PharmD for case-by-case management
Ibrutinib	Hold ibrutinib[1]
Cytotoxic chemotherapy	Contact oncology PharmD for case-by-case management
Miscellaneous	
Aliskiren	Hold aliskiren[1]
Apalutamide	Do not use Paxlovid
Bosentan	Do not use Paxlovid
Buspirone	Reduce buspirone dose by 50%[1]
Cilostazol	Reduce cilostozal dose to 50 mg BID; contact cardiology PharmD if unable[1]
Colchicine	Consider holding based on indication, monitor for signs of colchicine toxicity in patients with coexisting severe hepatic and renal impairment[1]
Darifenacin	Hold darifenacin[1]
Digoxin	Contact cardiology PharmD for case-by-case management based on indication
Domperidone	Hold domperidone[1]
Eluxadoline	Decrease dose to 75 mg BID[1] If not possible, do not use Paxlovid
Enzalutamide	Do not use Paxlovid
Flibanserin	Hold for two weeks after last dose of Paxlovid
Glecaprevir and pibrentasvir	Contact Hepatitis C specialist for case-by-case management
Ivabradine	Do not use Paxlovid
Lonafarnib	Do not use Paxlovid
Lomitapide	Do not use Paxlovid
Naloxegol	Hold naloxegol[1]
Ranolazine	Anti-anginal: hold ranolazine[1] Anti-arrhythmic: contact cardiology PharmD
Riociguat	Do not use Paxlovid

Miscellaneous	
Saxagliprin	Reduce saxagliptin 2.5 mg daily; hold saxagliptin or saxagliptin-containing combination product if unable[1]
Salmeterol	Hold salmeterol[1] Use alternative beta-2-agonist if unable to hold salmeterol
St. John's Wort	Do not use Paxlovid
Suvorexant	Hold suvorexant[1]
Tolvaptan	Consider alternatives or holding tolvaptan. Contact PharmD if unable to hold tolvaptan.
Trazodone	Reduce trazodone by 50%[1]
Voclosporin	Do not use Paxlovid
Vorapaxar	Hold vorapaxar[1]
Warfarin	Carefully monitor INR[1]

Appendix A

Preferred management of drug interactions of Paxlovid with calcineurin inhibitors and mTOR kinase inhibitors in recipients of solid organ or hematopoietic cell transplants

Checklist:

1) Contact transplant PharmD (Appendix B) to evaluate for **all** drug-drug interactions in table above and Liverpool reference. Avoid Paxlovid if absolute contraindications identified and holding interaction medication not possible.
2) **Hold all calcineurin inhibitors and mTOR inhibitors at time Paxlovid is written**
3) Start Paxlovid at 24 – 48 hours from time of last dose of CNI or mTOR inhibitor (see table below)
4) Check CNI or mTOR inhibitor level per table below and restart when appropriate

Drug	When to start Paxlovid	Check level
Envarsus	**48 hours** from last Envarsus dose	Day 3 – 7 **after** last day of Paxlovid
Tacrolimus	**24 hours** from last tacrolimus dose	Day 3 – 7 **after** last day of Paxlovid
Cyclosporine	**24 hours** from last cyclosporine dose	Day 3 – 7 **after** last day of Paxlovid
Everolimus	**48 hours** from last everolimus dose	Day 3 – 7 **after** last day of Paxlovid
Sirolumus	**48 hours** from last sirolimus dose	Day 3 – 7 **after** last day of Paxlovid

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Appendix B
Contact methods for pharmacists

Coverage:
0700 – 1600 Monday-Friday, except institutional holidays

Non-transplant patients:
For questions regarding drug-drug interactions that cannot be addressed by this guidance or the Liverpool website, please contact the pharmacist in your patient care area or the pharmacist involved in the care of that patient regarding the specific drug interaction. Please consider the timing of this medication as the response back from the clinical pharmacist may not be immediate. If no pharmacist is in the given patient care area, contact the Antimicrobial Stewardship Pharmacist (pg#31888).

Hematopoietic Cell Transplant Recipients:
Page David Frame, PharmD, Denise Markstrom, PharmD, or Gianni Scappaticci, PharmD

Solid Organ Transplant Recipients:

Transplant Program	Pharmacist Contact (MiChart In-basket Pool)
Adult Kidney	TC TXP PHARMACIST KP
Pediatric Kidney	TC TXP PHARMACIST KP
Adult Liver	TC TXP PHARMACIST LIV
Pediatric Liver	TC TXP PHARMACIST LIV
Lung	TC TXP PHARMACIST LUNG
	Pharmacist Contact via Email
Adult Heart	Sarah Hanigan, Kristin Pogue, or Claire Walter
Pediatric Heart	Audrey Jarosz or Ashley Huebschman

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P&T Approval: N/A	Last Revised: 02/2022

Revision History:
1/17/22: Added Appendices A and B
1/19/22: Revised general recommendation
1/20/22: Revised corticosteroid recommendation
2/15/22: Revised general recommendation
2/24/22: Updated CGRP antagonist
2/28/22: Revised multiple medications