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		
Generic name	*Trade names* (not all inclusive)	[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	*Biaxin*	Contact infectious diseases PharmD for case-by-case management based on indication
Erythromycin		Hold erythromycin[1]
Rifampin	*Rifadin*	Do not use Paxlovid
Rifapentine	*Priftin*	Do not use Paxlovid
Alpha-1 blockers		
Alfuzosin	*Uroxatral*	Hold alfuzosin[1]
Silodosin	*Rapaflo*	Hold silodosin[1]
Tamsulosin	*Flomax*	Hold tamsulosin[1]
Anti-arrhythmic (other than sotalol)		
Amiodarone	*Nexterone, Pacerone*	Do not use Paxlovid
Disopyramide	*Norpace*	Do not use Paxlovid
Dofetilide	*Tikosyn*	Do not use Paxlovid
Dronaderone	*Multaq*	Do not use Paxlovid
Flecainide	*Tambocor*	Do not use Paxlovid
Mexilitine		Do not use Paxlovid
Propafenone	*Rythmol*	Do not use Paxlovid
Quinidine		Do not use Paxlovid
Anti-epileptics		
Carbamazepine	*Carbatrol, Epitol, Equetro, Tegretol*	Do not use Paxlovid
Phenobarbital		Do not use Paxlovid
Phenytoin	*Dilantin, Phenytek*	Do not use Paxlovid
Primidone	*Mysoline*	Do not use Paxlovid
Antipsychotics		
Aripiprazole	*Abilify*	Reduce aripiprazole dose 50%, monitor for sedation, restlessness, dizziness, confusion[1]
Brexpiprazole	*Rexulti*	Reduce brexpiprazole dose 50%, monitor for sedation, restlessness, dizziness, confusion[1]
Cariprazine	*Vraylar*	Contact psychiatry PharmD for case-by-case management based on indication
Clozapine	*Clozaril, Versacloz*	Contact psychiatry PharmD
Iloperidone	*Fanapt*	Contact psychiatry PharmD for case-by-case management based on indication
Lumateperone	*Caplyta*	Do not use Paxlovid
Lurasidone	*Latuda*	Contact psychiatry PharmD for case-by-case management based on indication
Pimavenserin	*Nuplazid*	Reduce pimavenserin dose to 10 mg daily or hold if unable[1]
Pimozide		Do not use Paxlovid
Quetiapine	*Seroquel*	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	*Xanax*	Reduce alprazolam dose by 50%[1]
Chlordiazepoxide		Use with caution[1]
Clobazam	*Onfi, Sympazan*	Use with caution[1]
Clonazepam	*Klonopin*	Use with caution[1]
Clorazepate	*Tranxene-T*	Hold clorazepate UNLESS used for seizures[1] If used for seizure management, do not use Paxlovid
Diazepam	*Diastat, Valium, Valtoco*	Use with caution[1]
Estazolam		Hold estazolam[1]
Flurazepam	*Som-Pam*	Hold flurazepam[1]
Midazolam (oral)	*Nayzilam*	Do not use midazolam oral
Triazolam	*Halcion*	Do not use triazolam
Calcineurin inhibitors		
Cyclosporine	*Gengraf, Neoral, Sandimmune*	See **Appendix A** below for management recommendations.
Tacrolimus	*Astagraf, Envarsus, Prograf*	See **Appendix A** below for management recommendations.
Calcium Channel Blockers		
Amlodipine	*Norvasc*	Reduce dose by 50%[1]
Diltiazem	*Cardizem, Matzim, Taztia, Tiadylt, Tiazac*	Reduce dose by 50%[1]
Felodipine	*Plendil*	Reduce dose by 50%[1]
Nicardipine	*Cardene*	Reduce dose by 50%[1]
Nifedipine	*Procardia*	Reduce dose by 50%[1]
Verapamil	*Calan, Verelan*	Reduce dose by 50%[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	*Ubrelvy*	Hold ubrogepant[1]
Rimegepant	*Nurtec*	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	*Eliquis*	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	*Pradaxa*	Can co-administer with Paxlovid, with the following exceptions: • Indication is atrial fibrillation and CrCL of 30 to 50 mL/min: dose of dabigatran should be reduced to 75 mg twice daily • Indication is atrial fibrillation and CrCL <30 mL/min: Do not use Paxlovid. • Any other dabigatran indication with a CrCL <50 mL/min: Do not use Paxlovid.
Edoxaban	*Savaysa*	Reduce edoxaban dose to 30 mg daily[1]
Rivaroxaban	*Xarelto*	Do not use Paxlovid
Ergot alkaloids		
Dihydroergotamine	*D.H.E., Migranal, Trudhesa*	Do not use Paxlovid
Ergoloid mesylates		Do not use Paxlovid
Ergonovine		Do not use Paxlovid
Ergotamine	*Ergomar*	Do not use Paxlovid
Methylergonovine	*Methergine*	Do not use Paxlovid
Inhaled corticosteroids		
Beclomethasone	*Qvar*	No specific action needed; monitor for adverse events[1]
Budesonide	*Pulmicort*	No specific action needed; monitor for adverse events[1]
Ciclesonide	*Alvesco*	No specific action needed; monitor for adverse events[1]
Fluticasone	*Flovent*	No specific action needed; monitor for adverse events[1]
Mometasone	*Asmanex*	No specific action needed; monitor for adverse events[1]
Janus Kinase (JAK) Inhibitors		
Abrocitinib	*Cibinqo*	May be coadministered without dose adjustments
Baricitinib	*Olumiant*	May be coadministered without dose adjustments
Fedratinib	*Inrebic*	Reduce dose to 200 mg once daily[1]
Ruxolitinib	*Jakafi*	Reduce dose by 50% and administer twice daily[1]
Tofacitinib	*Xeljanz*	Reduce total daily dose by 50%[1]
Upadacitinib	*Rinvoq*	Recommended maximum maintenance dosage is 15 mg daily[1]
mTOR inhibitors		
Everolimus	*Afinitor, Zortress*	Oncology: See **Appendix A** below for management recommendations. Solid organ or hematopoietic cell transplant: See **Appendix A** below for management recommendations.
Sirolimus	*Rapamune*	Solid organ or hematopoietic cell transplant: See **Appendix A** below for management recommendations.

Opioids		
Codeine		Use codeine with caution, monitor carefully for signs of opioid overdose[1]
Fentanyl	*Actiq, Fentora, Lazanda, Subsys*	Reduce fentanyl dose by 50% while on Paxlovid, monitor carefully for signs of opioid overdose[1]
Hydrocodone	*Hysingla, Lortab, Verdrocet, Xodol*	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	*Demerol*	Use with caution[1]
Oxycodone	*Oxaydo, Oxycontin, Roxicodone, Xtampza, Endocet, Nalocet, Percocet*	Reduce oxycodone dose by 75%, monitor carefully for signs of opioid overdose[1]
Tramadol	*Conzip, Qdolo, Ultram*	Monitor carefully for signs of tramadol toxicity[1]
Potassium-sparing diuretics		
Eplerenone	*Inspra*	Do not use Paxlovid
Finerenone	*Kerendia*	Hold finerenone[1]
P2Y12 antagonists		
Clopidogrel	*Plavix*	Paxlovid reduces the effect of clopidogrel. Alternative therapy may be required depending on indication and timing of stent placement. Consult cardiologist/cardiac interventionalist for case-by-case management. Cardiology PharmD may assist as needed.
Ticagrelor	*Brilinta*	Do not use Paxlovid
Prasugrel	*Effient*	Can co-administer with Paxlovid
PDE5 inhibitors		
Avanafil	*Stendra*	Hold avanafil[1]
Sildenafil	*Viagra*	Erectile dysfunction, Raynaud phenomenon: hold sildenafil[1] Pulmonary hypertension, pulmonary edema: do not use Paxlovid
Tadalafil	*Adcirca, Alyq, Cialis*	BPH, erectile dysfunction, Raynaud phenomenon: hold tadalafil[1] Pulmonary hypertension: do not use Paxlovid
Vardenafil	*Levitra*	Erectile dysfunction, Raynaud phenomenon: hold vardenafil[1] Pulmonary hypertension: do not use Paxlovid
Statins		
Atorvastatin	*Lipitor*	Hold atorvastatin[1]
Lovastatin	*Altoprev*	Hold lovastatin[1]
Rosuvastatin	*Crestor*	Hold rosuvastatin[1]
Simvastatin	*Zocor*	Hold simvastatin[1]
Triptans		
Almotriptan	*Axert*	Use an initial dose of 6.25 mg and do not exceed 12.5 mg within a 24 hour period. Avoid use in patients with impaired renal or hepatic function[1]
Eletriptan	*Relpax*	Hold eletriptran[1]
Zolmitriptan	*Zomig*	Maximum dose 5 mg per day
Oral chemotherapy / small molecules Contact oncology PharmD for case-by-case management		
Ibrutinib	*Imbruvica*	Hold ibrutinib[1]
Cytotoxic chemotherapy		Contact oncology PharmD for case-by-case management

Miscellaneous		
Aliskiren	*Tekturna*	Hold aliskiren[1]
Apalutamide	Erleada	Do not use Paxlovid
Bosentan	*Tracleer*	Do not use Paxlovid
Brincidofovir	*Tembexa*	Give Paxlovid at least 3 hours after administration of brincidofovir
Buspirone	*Buspar*	Reduce buspirone dose by 50%[1]
Cilostazol	*Pletal*	Reduce cilostozal dose to 50 mg BID; contact cardiology PharmD if unable[1]
Colchicine	*Colcrys, Gloperba, Mitigare*	Consider holding based on indication, monitor for signs of colchicine toxicity in patients with coexisting severe hepatic and renal impairment[1]
Darifenacin	*Enablex*	Hold darifenacin[1]
Digoxin	*Digitek, Digox, Lanoxin*	Contact cardiology PharmD for case-by-case management based on indication
Domperidone		Hold domperidone[1]
Eluxadoline	*Viberzi*	Decrease dose to 75 mg BID[1] If not possible, do not use Paxlovid
Enzalutamide	*Xtandi*	Do not use Paxlovid
Flibanserin	*Addyi*	Hold for two weeks after last dose of Paxlovid
Glecaprevir and pibrentasvir	*Mavyret*	Contact Hepatitis C specialist for case-by-case management
Ivabradine	*Corlanor*	Do not use Paxlovid
Lonafarnib	*Zokinvy*	Do not use Paxlovid
Lomitapide	*Juxtapid*	Do not use Paxlovid
Naloxegol	*Movantik*	Hold naloxegol[1]
Oxybutnin	*Ditropan*	Monitor for anticholinergic adverse effects.[1] Do not use Paxlovid in elderly patients
Ranolazine	*Ranexa*	Anti-anginal: hold ranolazine[1] Anti-arrhythmic: contact cardiology PharmD
Riociguat	*Adempas*	Do not use Paxlovid
Saxagliptin	*Onglyza*	Reduce saxagliptin 2.5 mg daily; hold saxagliptin or saxagliptin-containing combination product if unable[1]
Salmeterol	*Serevent*	Hold salmeterol[1] Use alternative beta-2-agonist if unable to hold salmeterol
Solifenacin	*Vesicare*	Limit solifenacin dosage to 5 mg once daily[1]
St. John's Wort		Do not use Paxlovid
Suvorexant	*Belsomra*	Hold suvorexant[1]
Tolvaptan	*Jynarque, Samsca*	Consider alternatives or holding tolvaptan. Contact PharmD if unable to hold tolvaptan.
Trazodone	*Desyrel*	Reduce trazodone by 50%[1]
Voclosporin	*Lupkynis*	Do not use Paxlovid
Vorapaxar	*Zontivity*	Hold vorapaxar[1]
Warfarin	*Jantoven, Coumadin*	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

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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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
5/6/22: Revised DOACs
5/13/22: Added trade names
8/9/22: Revised ICS, added JAK inhibitors, triptans, brincidofovir, and oxybutinin
12/13/22: Removed mAb recommendations
7/19/23: Revised calcium channel blockers and P2Y12 antagonist recommendations

The recommendations in this guide are meant to serve as treatment guidelines for use at Michigan Medicine facilities. If you are an individual experiencing a medical emergency, call 911 immediately. These guidelines should not replace a provider's professional medical advice based on clinical judgment, or be used in lieu of an Infectious Diseases consultation when necessary. As a result of ongoing research, practice guidelines may from time to time change. The authors of these guidelines have made all attempts to ensure the accuracy based on current information, however, due to ongoing research, users of these guidelines are strongly encouraged to confirm the information contained within them through an independent source.

If obtained from a source other than med.umich.edu/asp, please visit the webpage for the most up-to-date document.