



## 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)	<sup>1</sup> Recommendation (inhibition resolves approximately 3 days after Paxlovid is discontinued. Unless otherwise stated, interacting medications should be managed (held/dose reduced/extra monitoring) 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)
<b>Antibiotics</b>		
<i>Clarithromycin</i>	<i>Biaxin</i>	Contact infectious diseases PharmD for case-by-case management based on indication
<i>Erythromycin</i>		Hold erythromycin <sup>1</sup>
<i>Rifampin</i>	<i>Rifadin</i>	Do not use Paxlovid
<i>Rifapentine</i>	<i>Priftin</i>	Do not use Paxlovid
<b>Alpha-1 blockers</b>		
<i>Alfuzosin</i>	<i>Uroxatral</i>	Hold alfuzosin <sup>1</sup>
<i>Silodosin</i>	<i>Rapaflo</i>	Hold silodosin <sup>1</sup>
<i>Tamsulosin</i>	<i>Flomax</i>	Hold tamsulosin <sup>1</sup>
<b>Anti-arrhythmic (other than sotalol)</b>		
<i>Amiodarone</i>	<i>Nexterone, Pacerone</i>	Do not use Paxlovid
<i>Disopyramide</i>	<i>Norpace</i>	Do not use Paxlovid
<i>Dofetilide</i>	<i>Tikosyn</i>	Do not use Paxlovid
<i>Dronedrone</i>	<i>Multaq</i>	Do not use Paxlovid
<i>Flecainide</i>	<i>Tambocor</i>	Do not use Paxlovid
<i>Mexilitine</i>		Do not use Paxlovid
<i>Propafenone</i>	<i>Rythmol</i>	Do not use Paxlovid
<i>Quinidine</i>		Do not use Paxlovid
<b>Anti-epileptics</b>		
<i>Carbamazepine</i>	<i>Carbatrol, Epitol, Equetro, Tegretol</i>	Do not use Paxlovid
<i>Phenobarbital</i>		Do not use Paxlovid
<i>Phenytoin</i>	<i>Dilantin, Phenytek</i>	Do not use Paxlovid
<i>Primidone</i>	<i>Mysoline</i>	Do not use Paxlovid
<b>Antipsychotics</b>		
<i>Aripiprazole</i>	<i>Abilify</i>	Reduce aripiprazole dose 50%, monitor for sedation, restlessness, dizziness, confusion <sup>1</sup>
<i>Brexpiprazole</i>	<i>Rexulti</i>	Reduce brexpiprazole dose 50%, monitor for sedation, restlessness, dizziness, confusion <sup>1</sup>
<i>Cariprazine</i>	<i>Vraylar</i>	Contact psychiatry PharmD for case-by-case management based on indication
<i>Clozapine</i>	<i>Clozaril, Versacloz</i>	Contact psychiatry PharmD
<i>Iloperidone</i>	<i>Fanapt</i>	Contact psychiatry PharmD for case-by-case management based on indication
<i>Lumateperone</i>	<i>Caplyta</i>	Do not use Paxlovid
<i>Lurasidone</i>	<i>Latuda</i>	Contact psychiatry PharmD for case-by-case management based on indication
<i>Pimavenserin</i>	<i>Nuplazid</i>	Reduce pimavenserin dose to 10 mg daily or hold if unable <sup>1</sup>
<i>Pimozide</i>		Do not use Paxlovid
<i>Quetiapine</i>	<i>Seroquel</i>	Contact psychiatry PharmD for case-by-case management based on indication

<b>Antiretrovirals</b>		
<i>HIV medications</i>		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 <a href="#">IDSA/ HIVMA brief</a>
<b>Benzodiazepines</b>		
<i>Alprazolam</i>	<i>Xanax</i>	Reduce alprazolam dose by 50% <sup>1</sup>
<i>Chlordiazepoxide</i>		Use with caution <sup>1</sup>
<i>Clobazam</i>	<i>Onfi, Sympazan</i>	Use with caution <sup>1</sup>
<i>Clonazepam</i>	<i>Klonopin</i>	Use with caution <sup>1</sup>
<i>Clorazepate</i>	<i>Tranxene-T</i>	Hold clorazepate UNLESS used for seizures <sup>1</sup> If used for seizure management, do not use Paxlovid
<i>Diazepam</i>	<i>Diastat, Valium, Valtoco</i>	Use with caution <sup>1</sup>
<i>Estazolam</i>		Hold estazolam <sup>1</sup>
<i>Flurazepam</i>	<i>Som-Pam</i>	Hold flurazepam <sup>1</sup>
<i>Midazolam (oral)</i>	<i>Nayzilam</i>	Do not use midazolam oral
<i>Triazolam</i>	<i>Halcion</i>	Do not use triazolam
<b>Calcineurin inhibitors</b>		
<i>Cyclosporine</i>	<i>Gengraf, Neoral, Sandimmune</i>	See <a href="#">Appendix A</a> below for management recommendations.
<i>Tacrolimus</i>	<i>Astagraf, Envarsus, Prograf</i>	See <a href="#">Appendix A</a> below for management recommendations.
<b>Calcium Channel Blockers</b>		
<i>Amlodipine</i>	<i>Norvasc</i>	Reduce dose by 50% <sup>1</sup>
<i>Diltiazem</i>	<i>Cardizem, Matzim, Taztia, Tiadylt, Tiazac</i>	Use with caution <sup>1</sup>
<i>Felodipine</i>	<i>Plendil</i>	Use with caution <sup>1</sup>
<i>Nicardipine</i>	<i>Cardene</i>	Use with caution <sup>1</sup>
<i>Nifedipine</i>	<i>Procardia</i>	Use with caution <sup>1</sup>
<i>Verapamil</i>	<i>Calan, Verelan</i>	Use with caution <sup>1</sup>
<b>CFTR Modulators</b>		
<i>Elexacaftor/tezacaftor/ivacaftor</i>	<i>Trikafta</i>	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
<i>Ivacaftor</i>	<i>Kalydeco</i>	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
<i>Tezacaftor/ivacaftor</i>	<i>Symdeko</i>	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
<i>Lumecaftor/ivacaftor</i>	<i>Orkambi</i>	Do not use Paxlovid
<b>CGRP Antagonist</b>		
<i>Ubrogepant</i>	<i>Ubrelvy</i>	Hold ubrogepant <sup>1</sup>
<i>Rimegepant</i>	<i>Nurtec</i>	Hold rimegepant <sup>1</sup>

<b>Corticosteroids (oral)</b>		<p>Standing corticosteroid: Consider reducing corticosteroid dose by 50-75% after weighing risk/benefit of short-term increase in steroid exposure</p> <p>Do NOT use oral corticosteroid for mild/moderate COVID-19 without hypoxia</p>
<b>Direct oral anticoagulants</b>		
<i>Apixaban</i>	<i>Eliquis</i>	<p>Doses &gt;2.5 mg BID: reduce apixaban dose by 50%<sup>1</sup></p> <p>Dose = 2.5 mg BID: Contact cardiology PharmD for case-by-case management based on indication</p>
<i>Dabigatran</i>	<i>Pradaxa</i>	<p>Can co-administer with Paxlovid, with the following exceptions:</p> <ul style="list-style-type: none"> <li>• Indication is atrial fibrillation and CrCL of 30 to 50 mL/min: dose of dabigatran should be reduced to 75 mg twice daily</li> <li>• Indication is atrial fibrillation and CrCL &lt;30 mL/min: Do not use Paxlovid.</li> <li>• Any other dabigatran indication with a CrCL &lt;50 mL/min: Do not use Paxlovid.</li> </ul>
<i>Edoxaban</i>	<i>Savaysa</i>	Reduce edoxaban dose to 30 mg daily <sup>1</sup>
<i>Rivaroxaban</i>	<i>Xarelto</i>	Do not use Paxlovid
<b>Ergot alkaloids</b>		
<i>Dihydroergotamine</i>	<i>D.H.E., Migranal, Trudhesa</i>	Do not use Paxlovid
<i>Ergoloid mesylates</i>		Do not use Paxlovid
<i>Ergonovine</i>		Do not use Paxlovid
<i>Ergotamine</i>	<i>Ergomar</i>	Do not use Paxlovid
<i>Methylergonovine</i>	<i>Methergine</i>	Do not use Paxlovid
<b>Inhaled corticosteroids</b>		
<i>Beclomethasone</i>	<i>Qvar</i>	No specific action needed; monitor for adverse events <sup>1</sup>
<i>Budesonide</i>	<i>Pulmicort</i>	No specific action needed; monitor for adverse events <sup>1</sup>
<i>Ciclesonide</i>	<i>Alvesco</i>	No specific action needed; monitor for adverse events <sup>1</sup>
<i>Fluticasone</i>	<i>Flovent</i>	No specific action needed; monitor for adverse events <sup>1</sup>
<i>Mometasone</i>	<i>Asmanex</i>	No specific action needed; monitor for adverse events <sup>1</sup>
<b>Janus Kinase (JAK) Inhibitors</b>		
<i>Abrocitinib</i>	<i>Cibinqo</i>	May be coadministered without dose adjustments
<i>Baricitinib</i>	<i>Olumiant</i>	May be coadministered without dose adjustments
<i>Fedratinib</i>	<i>Inrebic</i>	Reduce dose to 200 mg once daily <sup>1</sup>
<i>Ruxolitinib</i>	<i>Jakafi</i>	Reduce dose by 50% and administer twice daily <sup>1</sup>
<i>Tofacitinib</i>	<i>Xeljanz</i>	Reduce total daily dose by 50% <sup>1</sup>
<i>Upadacitinib</i>	<i>Rinvoq</i>	Recommended maximum maintenance dosage is 15 mg daily <sup>1</sup>
<b>mTOR inhibitors</b>		
<i>Everolimus</i>	<i>Afinitor, Zortress</i>	<p>Oncology: See <a href="#">Appendix A</a> below for management recommendations.</p> <p>Solid organ or hematopoietic cell transplant: See <a href="#">Appendix A</a> below for management recommendations.</p>
<i>Sirolimus</i>	<i>Rapamune</i>	Solid organ or hematopoietic cell transplant: See <a href="#">Appendix A</a> below for management recommendations.

<b>Opioids</b>		
<i>Codeine</i>		Use codeine with caution, monitor carefully for signs of opioid overdose <sup>1</sup>
<i>Fentanyl</i>	<i>Actiq, Fentora, Lazanda, Subsys</i>	Reduce fentanyl dose by 50% while on Paxlovid, monitor carefully for signs of opioid overdose <sup>1</sup>
<i>Hydrocodone</i>	<i>Hysingla, Lortab, Verdrocet, Xodol</i>	New start / PRN: consider reducing starting hydrocodone dose by 50%, monitor carefully <sup>1</sup>  Chronic maintenance: reduce hydrocodone dose by 50%, monitor carefully for signs of opioid overdose <sup>1</sup>
<i>Meperidine</i>	<i>Demerol</i>	Use with caution <sup>1</sup>
<i>Oxycodone</i>	<i>Oxaydo, Oxycotin, Roxicodone, Xtampza, Endocet, Nalocet, Percocet</i>	Reduce oxycodone dose by 75%, monitor carefully for signs of opioid overdose <sup>1</sup>
<i>Tramadol</i>	<i>Conzip, Qdolo, Ultram</i>	Monitor carefully for signs of tramadol toxicity <sup>1</sup>
<b>Potassium-sparing diuretics</b>		
<i>Eplerenone</i>	<i>Inspra</i>	Do not use Paxlovid
<i>Finerenone</i>	<i>Kerendia</i>	Hold finerenone <sup>1</sup>
<b>P2Y12 antagonists</b>		
<i>Clopidogrel</i>	<i>Plavix</i>	Contact cardiology PharmD for case-by-case management based on indication and timing of stent placement
<i>Ticagrelor</i>	<i>Brilinta</i>	Contact cardiology PharmD for case-by-case management based on indication and timing of stent placement
<i>Prasugrel</i>	<i>Effient</i>	Can co-administer with Paxlovid
<b>PDE5 inhibitors</b>		
<i>Avanafil</i>	<i>Stendra</i>	Hold avanafil <sup>1</sup>
<i>Sildenafil</i>	<i>Viagra</i>	Erectile dysfunction, Raynaud phenomenon: hold sildenafil <sup>1</sup> Pulmonary hypertension, pulmonary edema: do not use Paxlovid
<i>Tadalafil</i>	<i>Adcirca, Alyq, Cialis</i>	BPH, erectile dysfunction, Raynaud phenomenon: hold tadalafil <sup>1</sup> Pulmonary hypertension: do not use Paxlovid
<i>Vardenafil</i>	<i>Levitra</i>	Erectile dysfunction, Raynaud phenomenon: hold vardenafil <sup>1</sup> Pulmonary hypertension: do not use Paxlovid
<b>Statins</b>		
<i>Atorvastatin</i>	<i>Lipitor</i>	Hold atorvastatin <sup>1</sup>
<i>Lovastatin</i>	<i>Altoprev</i>	Hold lovastatin <sup>1</sup>
<i>Rosuvastatin</i>	<i>Crestor</i>	Hold rosuvastatin <sup>1</sup>
<i>Simvastatin</i>	<i>Zocor</i>	Hold simvastatin <sup>1</sup>
<b>Triptans</b>		
<i>Almotriptan</i>	<i>Axert</i>	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 <sup>1</sup>
<i>Eletriptan</i>	<i>Relpax</i>	Hold eletriptan <sup>1</sup>
<i>Zolmitriptan</i>	<i>Zomig</i>	Maximum dose 5 mg per day
<b>Oral chemotherapy / small molecules</b>		
Contact oncology PharmD for case-by-case management		
<i>Ibrutinib</i>	<i>Imbruvica</i>	Hold ibrutinib <sup>1</sup>
<b>Cytotoxic chemotherapy</b>		
Contact oncology PharmD for case-by-case management		

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

**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	<b>48 hours</b> from last Envarsus dose	Day 3 – 7 <b>after</b> last day of Paxlovid
Tacrolimus	<b>24 hours</b> from last tacrolimus dose	Day 3 – 7 <b>after</b> last day of Paxlovid
Cyclosporine	<b>24 hours</b> from last cyclosporine dose	Day 3 – 7 <b>after</b> last day of Paxlovid
Everolimus	<b>48 hours</b> from last everolimus dose	Day 3 – 7 <b>after</b> last day of Paxlovid
Sirolimus	<b>48 hours</b> from last sirolimus dose	Day 3 – 7 <b>after</b> 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
<b>Pharmacist Contact via Email</b>	
Adult Heart	Sarah Hanigan, Kristin Pogue, or Claire Walter
Pediatric Heart	Audrey Jarosz or Ashley Huebschman

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*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.*

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