

MANAGEMENT OF PAXLOVID (nirmatrelvir-ritonavir) 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.

Paxlovid is a strong CYP3A4 inhibitor: 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)

PAXLOVID is contraindicated with drugs that are highly dependent on CYP3A for clearance and for which elevated concentrations are associated with serious and/or life-threatening reactions:

- Alpha1-adrenoreceptor antagonist: alfuzosin
- Antianginal: ranolazine
- Antiarrhythmic: amiodarone, dronedarone, flecainide, propafenone, quinidine
- Anti-gout: colchicine
- **Antipsychotics: lurasidone, pimozide**
- Benign prostatic hyperplasia agents: silodosin
- Cardiovascular agents: eplerenone, ivabradine
- Ergot derivatives: dihydroergotamine, ergotamine, methylergonovine
- HMG-CoA reductase inhibitors: lovastatin, simvastatin
- Immunosuppressants: voclosporin
- Microsomal triglyceride transfer protein inhibitor: lomitapide
- Migraine medications: eletriptan, ubrogepant
- Mineralocorticoid receptor antagonists: finerenone
- Opioid antagonists: naloxegol
- PDE5 inhibitor: sildenafil (Revatio®) when used for pulmonary arterial hypertension (PAH)
- **Sedative/hypnotics: triazolam, oral midazolam**
- Serotonin receptor 1A agonist/serotonin receptor 2A antagonist: flibanserin
- Vasopressin receptor antagonists: tolvaptan

PAXLOVID is contraindicated with drugs that are potent CYP3A inducers where significantly reduced nirmatrelvir or ritonavir plasma concentrations may be associated with the potential for loss of virologic response and possible resistance. PAXLOVID cannot be started immediately after discontinuation of any of the following medications due to the delayed offset of the recently discontinued CYP3A inducer:

- Anticancer drugs: apalutamide
- Anticonvulsant: **carbamazepine**, phenobarbital, primidone, phenytoin
- Cystic fibrosis transmembrane conductance regulator potentiators: lumacaftor/ivacaftor
- Antimycobacterials: rifampin
- **Herbal products: St. John's Wort (hypericum perforatum)**

Drug Class	Generic Name	Trade Name	Clinical Comments
Anticonvulsants			
	Carbamazepine	Carbatrol, Epitol, Equetro, Tegretol	Do not use Paxlovid. Co-administration contraindicated due to potential loss of virologic response and possible resistance.
Antidepressants			
	Bupropion		Monitor for an adequate clinical response to bupropion.
	Tazodone	Desyrel	Reduce trazodone by 50%. Adverse reactions of nausea, dizziness, hypotension, and syncope have been observed following co-administration of trazodone and ritonavir. A lower dose of trazodone should be considered. Refer to trazodone product label for further information.

Antipsychotics

Aripiprazole	Abilify	Reduce aripiprazole dose 50%, monitor for sedation, restlessness, dizziness, confusion. Dosage adjustment of aripiprazole, brexpiprazole, cariprazine, iloperidone, lumateperone, and pimavanserin is recommended. Refer to individual product label for more information.
Brexpiprazole	Rexulti	Reduce brexpiprazole dose 50%, monitor for sedation, restlessness, dizziness, confusion. Dosage adjustment of aripiprazole, brexpiprazole, cariprazine, iloperidone, lumateperone, and pimavanserin is recommended. Refer to individual product label for more information.
Cariprazine	Vraylar	Dosage adjustment is recommended. Dosage adjustment of aripiprazole, brexpiprazole, cariprazine, iloperidone, lumateperone, and pimavanserin is recommended. Refer to individual product label for more information.
Clozapine	Clozaril, Versacloz	Do not use Paxlovid. If co-administration is necessary, consider reducing the clozapine dose and monitor for adverse reactions.
Iloperidone	Fanapt	Dosage adjustment is recommended. Dosage adjustment of aripiprazole, brexpiprazole, cariprazine, iloperidone, lumateperone, and pimavanserin is recommended. Refer to individual product label for more information.
Lumateperone	Caplyta	Reduce lumateperone dose 50%. Dosage adjustment of aripiprazole, brexpiprazole, cariprazine, iloperidone, lumateperone, and pimavanserin is recommended. Refer to individual product label for more information.
Lurasidone	Latuda	Co-administration contraindicated due to serious and/or life-threatening reactions such as cardiac arrhythmias.
Pimavanserin	Nuplazid	Reduce pimavanserin dose to 10 mg daily or hold if unable. Dosage adjustment of aripiprazole, brexpiprazole, cariprazine, iloperidone, lumateperone, and pimavanserin is recommended. Refer to individual product label for more information.
Pimozide		Do not use Paxlovid: Co-administration contraindicated due to serious and/or life-threatening reactions such as cardiac arrhythmias.
Quetiapine	Seroquel	If co-administration is necessary, reduce quetiapine dose and monitor for quetiapine-associated adverse reactions. Refer to the quetiapine prescribing information for recommendations.
Suvorexant	Belsomra	Hold Suvorexant. Avoid concomitant use of suvorexant with PAXLOVID.

Benzodiazepines

Alprazolam	Xanax	Reduce alprazolam dose by 50%
Chlordiazepoxide		Use with caution.
Clobazam	Onfi, Sympazan	Use with caution.
Clonazepam	Klonopin	Use with caution. A dose decrease may be needed for clonazepam when co-administered with PAXLOVID and clinical monitoring is recommended.
Clorazepate	Tranxene-T	Hold clorazepate UNLESS used for seizures. If used for seizure management, do not use Paxlovid. A dose decrease may be needed for these drugs when co-administered with PAXLOVID and monitoring for adverse events.
Diazepam	Diastat, Valium, Valtoco	Use with caution. A dose decrease may be needed for these drugs when co-administered with PAXLOVID and monitoring for adverse events.
Estazolam		Hold estazolam. A dose decrease may be needed for these drugs when co-administered with PAXLOVID and monitoring for adverse events.
Flurazepam	Som-Pam	Hold flurazepam. A dose decrease may be needed for these drugs when co-administered with PAXLOVID and monitoring for adverse events.
Midazolam (oral)	Nayzilam	Do not use midazolam oral. Co-administration of midazolam (parenteral) should be done in a setting which ensures close clinical monitoring and appropriate medical management in case of respiratory depression and/or prolonged sedation. Dosage reduction for midazolam should be considered, especially if more than a single dose of midazolam is administered. Refer to the midazolam product label for further information.
Triazolam	Halcion	Do not use triazolam. Co-administration contraindicated due to potential for extreme sedation and respiratory depression.
Zolpidem		A dose decrease may be needed for these drugs when co-administered with PAXLOVID and monitoring for adverse events.

Herbal products

St. John's Wort (hypericum perforatum)		Do not use Paxlovid. Co-administration contraindicated due to potential loss of virologic response and possible resistance
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References:

<https://www.fda.gov/media/155050/download>

https://www.med.umich.edu/asp/pdf/outpatient_guidelines/Paxlovid-DDI.pdf

Micromedex accessed 9/23/2022