

PROVIDER HEALTH ADVISORY

Date: March 3, 2022

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Prescribing Paxlovid (COVID-19 Treatment)

Paxlovid Updates:

- Eligibility has expanded to all Tiers (1-4) of the <u>NIH Treatment Guidelines on Patient</u> <u>Prioritization</u>.
- Now available widely in 7 pharmacies across SLO County, with 3 more coming soon.
- The COVID-19 Treatment Guidelines Panel recommends Paxlovid as first-choice treatment

1. Paxlovid Overview

Paxlovid[™] (nirmatrelvir tablets and ritonavir tablets, co-packaged for oral use) is an antiviral medication under Emergency Use Authorization (EUA) as an outpatient treatment for COVID-19. The 5-day course of treatment should be started as soon as COVID-19 is diagnosed and within 5 days of symptom onset. Paxlovid tablets (2 pink 150 mg tabs nirmtrelvir, 1 white 100 mg tablet ritonavir) are taken twice daily for 5 days, with or without food. Prescriptions should specify the numeric dose of each active ingredient within Paxlovid.

2. Who is eligible to receive a prescription for Paxlovid?

Under its EUA, this treatment may be prescribed to individuals ages 12 and older weighing at least 40 kg, with mild to moderate symptomatic COVID-19 who are at high risk for progression to severe disease. Timely prescription and treatment with Paxlovid is crucial as patients who are already admitted to the hospital with COVID-19 are no longer eligible. Paxlovid is not intended for use in preventing COVID-19.

3. Which medical conditions can increase one's risk of severe COVID-19?

The CDC has updated the <u>list of certain underlying medical conditions</u> that are associated with a higher risk for severe COVID-19 outcomes. This includes:

- Cancer
- Cerebrovascular Disease
- Chronic Kidney Disease
- Chronic Lung Diseases (limited to Interstitial Lung Disease, Pulmonary Embolism, Pulmonary HTN, Bronchiectasis, COPD
- Chronic Liver Diseases (Limited to Cirrhosis, NALFD, Alcoholic Liver Disease, Autoimmune Hepatitis)
- Cystic Fibrosis
- Diabetes Mellitus (Type 1 and Type 2)

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- Disabilities (see complete listing)
- Heart Conditions (CAD, CHF and Cardiomyopathies)
- HIV
- Mood Disorders (including Depression and Schizophrenia spectrum disorders)
- Dementia
- Obesity (BMI≥30kg/m²)
- Primary Immunodeficiencies
- Pregnancy and recent Pregnancy
- Physical Inactivity
- Smoking, current and former
- Solid organ or hematopoietic cell transplantation
- Tuberculosis
- Use of corticosteroids or other immunosuppressive medications

With available supply, **Public Health has now expanded eligibility to include Tiers 1-4** of the <u>NIH Treatment Guidelines on Patient Prioritization</u>:

Risk Group
• Immunocompromised individuals not expected to mount an adequate immune response to COVID-19 vaccination or SARS-CoV-2 infection due to their underlying conditions, regardless of vaccine status (see Immunocompromising Conditions below); <i>or</i>
 Unvaccinated individuals at the highest risk of severe disease (anyone aged ≥75 years or anyone aged ≥65 years with additional risk factors).
• Unvaccinated individuals at risk of severe disease not included in Tier 1 (anyone aged ≥65 years or anyone aged <65 years with clinical risk factors)
 Vaccinated individuals at high risk of severe disease (anyone aged ≥75 years or anyone aged ≥65 years with clinical risk factors)
Note: Vaccinated individuals who have not received a COVID-19 vaccine booster dose are likely at higher risk for severe disease; patients in this situation within this tier should be prioritized for treatment.
 Vaccinated individuals at risk of severe disease (anyone aged ≥65 years or anyone aged <65 with clinical risk factors)
Note: Vaccinated individuals who have not received a COVID-19 vaccine booster dose are likely at higher risk for severe disease; patients in this situation within this tier should be prioritized for treatment.

Source: <u>www.covid19treatmentguidelines.nih.gov/therapies/statement-on-patient-prioritization-for-outpatient-therapies</u>

4. Can patients with renal impairment take Paxlovid?

No dosage adjustment is needed in patients with mild renal impairment (eGFR \geq 60 to \leq 90). For moderate renal impairment (eGFR \geq 30 to <60) the dosage of Paxlovid is 150mg nirmatrelvir and 100 mg ritonavir twice daily for five days. Prescriptions for Paxlovid should specify the numeric

dose of each active ingredient within Paxlovid. Paxlovid is not recommended for patients with severe renal impairment.

5. Can patients with liver issues take Paxlovid?

For mild or moderate hepatic impairment (Child-Pugh Classes A & B), no adjustment of dosing is required. However, Paxlovid is not recommended for patients with *severe* hepatic impairment.

• Caution should be used when administering Paxlovid to patents with pre-existing liver diseases, liver enzyme abnormalities, or hepatitis because patients receiving ritonavir have experienced hepatic transaminase elevations, clinical hepatitis, and jaundice.

6. What are the contraindications for using Paxlovid?

- Severe hypersensitivity reactions to nirmetrelvir or ritonavir are a **contraindication** to using Paxlovid.
- Paxlovid is a CYP3A inhibitor. Co-administration of Paxlovid with other drugs that are dependent on CYP3A for clearance may require a dose adjustment or additional monitoring. (See full listing in the Fact Sheet for Healthcare Providers)
- The following drugs are highly dependent on **CYP3A** for clearance and their use with Paxlovid is **contraindicated**:
 - o Alfuzosin
 - Analgesics: pethidine, piroxicam, propoxyphene
 - Antianginal: ranolazine
 - Antiarrhythmic: amiodarone, dronedarone, flecainide, propafenone, quinidine
 - Antipsychotics: lurasidone, pimozide, clozapine
 - Ergot derivatives: dihydroergotamine, ergotamine, methylergonovine
 - HMG-CoA reductase inhibitors; lovastatin, simvastatin
 - PDE5 inhibitor: sildenafil when used for pulmonary arterial hypertension (PAH)
 - Sedative/hypnotics: triazolam, oral midazolam
- Paxlovid use is **contraindicated** immediately after discontinuation of the following medications:
 - Apalutamide (Anticancer)
 - Anticonvulsants: carbamazepine, phenobarbital, phenytoin
 - Antimycobacterials: rifampin
 - St. John's Wort (hypericum perforatum)

[For precautions, see Precautions Table pgs. 5-8]

7. What about patients who are pregnant, breastfeeding or using hormonal contraceptives?

Under its emergency use authorization, Paxlovid is not recommended for pregnant or breastfeeding individuals at this time. Paxlovid may also reduce the effectiveness of combined hormonal contraceptive, so patients prescribed Paxlovid should use a backup contraceptive method for the duration of the treatment.

8. Are there any side effects of Paxlovid?

Adverse events that occurred at a greater frequency in patients taking Paxlovid were dysgeusia, diarrhea, hypertension and myalgia.

9. Where can my patients currently get Paxlovid in SLO County?

Patients can currently fill Paxlovid prescriptions at seven pharmacies in SLO County:

- <u>Rite Aid Atascadero</u> (7025 El Camino Real in Atascadero, 805-466-8722)
- Rite Aid Paso Robles (1151 Creston Rd, Paso Robles 93446, 805-239-3028)
- <u>Rite Aid San Luis Obispo</u> (1251 Johnson Ave in San Luis Obispo, 805-545-0655)
- Vons San Luis Obispo (3900 Broad Street in San Luis Obispo, 805-541-1132)
- <u>Cayucos Pharmacy</u> (72 S. Ocean Avenue in Cayucos, 805-995-3538)
- <u>CVS Nipomo</u> (610 W Tefft ST, Nipomo 93444, 805-929-2740)
- <u>Best Care Arroyo Grande</u> (1690 E Grand Ave, Arroyo Grande, 805-474-0469)

The following three pharmacies will soon be carrying Paxlovid:

- <u>CVS Paso Robles</u> (187 Niblick Rd, Paso Robles 93466, 805-238-2947)
- <u>CVS San Luis Obispo</u> (1300 Madonna Rd, San Luis Obispo 93405, 805-549-0993)
- <u>Rite Aid Arroyo Grande</u> (1690 E Grand Ave, Arroyo Grande, 805-474-0469)

<u>Community Health Centers of the Central Coast</u> (CHC) is providing Paxlovid for CHC patients.

For More Information:

Paxlovid Fact Sheet for Health Care Providers: <u>www.fda.gov/media/155050/download</u>

COVID-19 Therapeutics and Treatment information: <u>www.slopublichealth.org/treatments</u>

SLO County COVID-19 website: www.slopublichealth.org/covid19

Drug Class	Drugs within Class	Effect on Concentration	Clinical Comments
Antiarrhythmics	bepridil, lidocaine (systemic)	↑ antiarrhythmic	Caution is warranted and therapeutic concentration monitoring is recommended for antiarrhythmics if available.
Anticancer drugs	abemaciclib, ceritinib, dasatinib, encorafenib, ibrutinib, ivosidenib, neratinib, nilotinib, venetoclax, vinblastine, vincristine	↑ anticancer drug	Avoid co-administration of encorafenib or ivosidenib due to potential risk of serious adverse events such as QT interval prolongation. Avoid use of neratinib, venetoclax or ibrutinib. Co-administration of vincristine and vinblastine may lead to significant hematologic or gastrointestinal side effects. For further information, refer to individual product label for anticancer drug.
Anticoagulants	warfarin	↑↓ warfarin	Closely monitor INR if co-administration with warfarin is necessary.
	rivaroxaban	↑ rivaroxaban	Increased bleeding risk with rivaroxaban. Avoid concomitant use.
Anticonvulsants	carbamazepine <u>*</u> , phenobarbital, phenytoin	↓ nirmatrelvir/ritonavir ↑ carbamazepine ↓ phenobarbital ↓ phenytoin	Co-administration contraindicated due to potential loss of virologic response and possible resistance <i>[see <u>Contraindications (4)</u>]</i> .
Antidepressants	bupropion	↓ bupropion and active metabolite hydroxy- bupropion	Monitor for an adequate clinical response to bupropion.
	trazodone	↑ trazodone	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 trazadone product label for further information.
Antifungals	voriconazole,	↓ voriconazole	Avoid concomitant use of voriconazole.
	ketoconazole, isavuconazonium sulfate itraconazole <u>*</u>	↑ ketoconazole ↑ isavuconazonium sulfate ↑ itraconazole ↑ nirmatrelvir/ritonavir	Refer to ketoconazole, isavuconazonium sulfate, and itraconazole product labels for further information.
Anti-HIV protease inhibitors	amprenavir, atazanavir,	↑ protease Inhibitor	For further information, refer to the respective protease inhibitors'

Drug Class	Drugs within Class	Effect on Concentration	Clinical Comments
	darunavir, fosamprenavir, indinavir, nelfinavir, saquinavir, tipranavir		prescribing information. Patients on ritonavir- or cobicistat- containing HIV regimens should continue their treatment as indicated. Monitor for increased PAXLOVID or protease inhibitor adverse events with concomitant use of these protease inhibitors [see Dosage and Administration (2.4)].
Anti-HIV	didanosine, delavirdine, efavirenz, maraviroc, nevirapine, raltegravir, zidovudine bictegravir/ emtricitabine/ tenofovir	 ↑ didanosine ↑ efavirenz ↑ maraviroc ↓ raltegravir ↓ zidovudine ↑ bictegravir ↔ emtricitabine ↑ tenofovir 	For further information, refer to the respective anti-HIV drugs prescribing information.
Anti-infective	clarithromycin, erythromycin	↑ clarithromycin ↑ erythromycin	Refer to the respective prescribing information for anti-infective dose adjustment.
Antimycobacterial	bedaquiline	↑ bedaquiline	Refer to the bedaquiline product label for further information.
	rifabutin	↑ rifabutin	Refer to rifabutin product label for further information on rifabutin dose reduction.
Antipsychotics	quetiapine	† quetiapine	If co-administration is necessary, reduce quetiapine dose and monitor for quetiapine-associated adverse reactions. Refer to the quetiapine prescribing information for recommendations.
Calcium channel blockers	amlodipine, diltiazem, felodipine, nicardipine, nifedipine	† calcium channel blocker	Caution is warranted and clinical monitoring of patients is recommended. A dose decrease may be needed for these drugs when co- administered with PAXLOVID. If co-administered, refer to individual product label for calcium channel blocker for further information.
Cardiac glycosides	digoxin	↑ digoxin	Caution should be exercised when co- administering PAXLOVID with digoxin, with appropriate monitoring of serum

Drug Class	Drugs within Class	Effect on Concentration	Clinical Comments
			digoxin levels. Refer to the digoxin product label for further information.
Endothelin receptor Antagonists	bosentan	↑ bosentan	Discontinue use of bosentan at least 36 hours prior to initiation of PAXLOVID. Refer to the bosentan product label for further information.
Hepatitis C direct acting antivirals	elbasvir/grazoprevir, glecaprevir/pibrentasvir ombitasvir/paritaprevir/	↑ antiviral	Increased grazoprevir concentrations can result in ALT elevations. It is not recommended to co-administer ritonavir with glecaprevir/pibrentasvir. Refer to the ombitasvir/paritaprevir/ritonavir and
	ritonavir and dasabuvir sofosbuvir/velpatasvir/v oxilaprevir		dasabuvir label for further information. Refer to the sofosbuvir/velpatasvir/voxilaprevir product label for further information. Patients on ritonavir-containing HCV regimens should continue their treatment as indicated. Monitor for increased PAXLOVID or HCV drug adverse events with concomitant use <i>[see Dosage and Administration (2.4)]</i> .
HMG-CoA reductase inhibitors	atorvastatin, rosuvastatin	↑ atorvastatin ↑ rosuvastatin	Consider temporary discontinuation of atorvastatin and rosuvastatin during treatment with PAXLOVID.
Hormonal contraceptive	ethinyl estradiol	↓ ethinyl estradiol	An additional, non-hormonal method of contraception should be considered.
Immunosuppressants	cyclosporine, tacrolimus, sirolimus	↑ cyclosporine ↑ tacrolimus ↑ sirolimus	 Therapeutic concentration monitoring is recommended for immunosuppressants. Avoid use of PAXLOVID when close monitoring of immunosuppressant serum concentrations is not feasible. Avoid concomitant use of sirolimus and PAXLOVID. If co-administered, refer to individual product label for immunosuppressant for further information.
Long-acting beta- adrenoceptor agonist	salmeterol	↑ salmeterol	Co-administration is not recommended. The combination may result in increased risk of cardiovascular adverse events associated with salmeterol,

Drug Class	Drugs within Class	Effect on Concentration	Clinical Comments
			including QT prolongation, palpitations, and sinus tachycardia.
Narcotic analgesics	fentanyl	↑ fentanyl	Careful monitoring of therapeutic and adverse effects (including potentially fatal respiratory depression) is recommended when fentanyl is concomitantly administered with PAXLOVID.
	methadone	↓ methadone	Monitor methadone-maintained patients closely for evidence of withdrawal effects and adjust the methadone dose accordingly.
Sedative/hypnotics	midazolam (administered parenterally)	↑ midazolam	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.
Systemic corticosteroids	betamethasone, budesonide, ciclesonide, dexamethasone, fluticasone, methylprednisolone, mometasone, prednisone, triamcinolone	↑ corticosteroid	Increased risk for Cushing's syndrome and adrenal suppression. Alternative corticosteroids including beclomethasone and prednisolone should be considered.