**A Prescription Guide for Providers**

**PAXLOVID** is a combination of nirmatrelvir and ritonavir protease inhibitors issued under Emergency Use Authorization (EUA) for treatment of mild to moderate COVID-19 in adults and children older than 12 years and weighing at least 40 kg. Nirmatrelvir inhibits the SARS-CoV-2 main protease preventing viral replication. Ritonavir inhibits the CYP3A-mediated metabolism of nirmatrelvir, resulting in increased plasma concentrations of nirmatrelvir.

The medication has EUA for those at high risk for progression to severe COVID-19, including hospitalization and death. PAXLOVID is not authorized for patients requiring hospitalization or for pre-exposure or post-exposure prophylaxis.

**Dosage and Administration**

- **Initiate as soon as possible after diagnosis of COVID-19 and within 5 days** of symptom onset.
- **300 mg (two 150-mg tablets) nirmatrelvir and one 100-mg tablet ritonavir all taken together twice daily for 5 days.**
- For moderate renal impairment (eGFR >30 to <60 mL/min): 150 mg nirmatrelvir (one 150-mg tablet) with 100 mg ritonavir (one 100-mg tablet) taken together twice daily for 5 days.
- **PAXLOVID is not recommended in patients with severe renal impairment (eGFR <30 mL/min) or severe hepatic impairment (Child Pugh Class C).**
- Take with or without food. Swallow all tablets whole – do not chew, break, or crush tablets.
- If a dose is missed within 8 hours, take as soon as possible and resume normal dosing schedule. If missed by more than 8 hours, do not take the missed dose. Instead take the next dose at the regularly scheduled time.

**Contraindications and Interactions**

The following list of contraindications and interactions is not exhaustive. Consult the package insert or fact sheet for detailed information, risk assessment, and mitigations.

**Special attention is required for potential drug interactions.** Be aware of co-administration with drugs highly dependent on CYP3A for clearance, for which elevated concentrations are associated with serious reactions. Drugs that induce CYP3A may decrease nirmatrelvir and ritonavir plasma concentrations and reduce PAXLOVID therapeutic effect.

The majority of drug interactions can be handled with discontinuing medications for a short period of time or notifying patients of potential side effects. Close consultation with the University of Liverpool Drug Interaction Tool is beneficial.

**University of Liverpool COVID-19 Drug Interaction Tool** (www.covid19-druginteractions.org/checker):

- Type proposed COVID-19 drug, Paxlovid, in the left column and click to select the drug.
- Type Co-medication(s) (generic name) patient currently taking and click to select each drug.
- Potential drug interactions will be displayed in the column at the right. Select "more info" to show the quality of evidence, summary and description of drug interaction(s).

Greatest concern for serious drug interactions involve anticoagulant, antiarhythmic, and immunosuppressives such as tacrolimus. Consider remdesivir IV as an option.
**Contraindications and Interactions (Continued)**

**PAXLOVID cannot be started immediately after discontinuation** of the following drugs due to delayed offset of the recently discontinued CYP3PA inducer:

- **Anti-cancer drugs**: apalutamide, **Anti-convulsant**: carbamazepine, phenobarbital, phenytoin, **Anti-mycobacterial**: rifampin, **Herbal** products: St. John’s Wort (hypericum)

**Established and other potentially significant drug interactions include but are not limited to the following:**

- **Anticoagulants** - warfarin, rivaroxaban; **Antidepressants** - bupropion, trazodone; **Antifungals** - voriconazole, ketoconazole, itraconazole; **Calcium Channel Blockers** - amlodipine, diltiazem, nefedipine, felodipine, nicardipine; **Cardiac Glycosides** - digoxin; **Endothelial Receptor Antagonists** - bosentan; **Anti-Gout** - colchicine; **Anti-HIV Protease Inhibitors** - amprenavir, atazanavir, darunavir, **Anti-HIV** - didanosine, efavirenz, maraviroc, raltegravir, bictegravir/ emtricitabine/ tenofovir; **Anti-Infective** - clarithromycin, erythromycin, rifabutin; **Anti-Hepatitis C** - elbasvir/grazoprevir, glecaprevir/pibrentasvir, ombitasvir/paritaprevir/ritonavir and dasabuvir, sofosbuvir/velpatasvir/ voxilaprevir; **Hormonal Contraceptives** - ethinyl estradiol; **Immunosuppressives** - cyclosporine, tacrolimus, sirolimus; **Long Acting Beta Adrenoceptor Agonist** - salmeterol; **Narcotic Analgesics** - fentanyl, methadone; **PDE5 Inhibitor** - sildenafil (when used for pulmonary artery hypertension); **Systemic Corticosteroids** – betamethasone, dexamethasone, budesonide, prednisone, triamcinolone.

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### Additional Information & Resources

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<th>Summary</th>
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<td><strong>Pregnancy</strong></td>
<td>Case series of 47 pregnant patients showed Paxlovid was well tolerated without evidence of an increase in complications affecting birthing parents or their offspring. Protease medications have been used for decades in HIV pregnant patients with no significant adverse events. Lactation is not a contraindication for the use of Paxlovid. Lactating individuals with one or more risk factors for severe disease may receive Paxlovid for treatment. Ritonavir may reduce the efficacy of combined hormonal contraceptives.</td>
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<td><strong>Efficacy</strong></td>
<td>The relative risk reduction for PAXLOVID relative to placebo was 88%. The EPIC-HR Phase 2/3 trial involved individuals with at least one risk factor for progression to severe disease, with an endpoint of COVID-19 related hospitalizations or death from any cause. The primary SARS-CoV-2 variant was Delta (98%).</td>
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<tr>
<td><strong>Patient Checklist Tool for Prescribers</strong></td>
<td>This checklist is intended as an aid to support clinical decision making for prescribers. However, use of this checklist is not required to prescribe PAXLOVID under the EUA.</td>
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<td><strong>Fact Sheet for Prescribers</strong></td>
<td>FDA Emergency Use Authorization for Paxlovid</td>
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<td><strong>Fact Sheet for Patients/Caregivers</strong></td>
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For the latest updates on COVID-19, visit: [www.sandiegocounty.gov/COVIDHealthProfessionals](http://www.sandiegocounty.gov/COVIDHealthProfessionals)