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LIVE WELL SAN DIEGO

PAXLOVID INFORMATIONAL SHEET SUMMARY

ORAL ANTIVIRAL MEDICATIONS TO TREAT MILD TO MODERATE COVID-19

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* to potential drug interactions. Be aware of co-administration with drugs highly dependent on CYP3A for clearance, for which elevated concentrations are associated with serious life-threatening reactions, and potent CYP3A inducers, where reduced nirmatrelvir or ritonavir plasma concentration may be associated with the potential for the loss of virologic response and possible resistance.

Examples of drugs contraindicated that are highly dependent on CYP3A for clearance and for which elevated concentrations are associated with serious and/or life-threatening reactions including hospitalization and death:

- Alpha-1 (α_1) adrenoreceptor antagonist: alfuzosin
- Analgesics: pethidine, piroxicam, propoxyphene
- Anti-anginal: ranolazine
- Anti-arrhythmic: amiodarone, dronedarone, flecainide, propafenone, quinidine
- Anti-gout: colchicine
- Antipsychotics: lurasidone, pimozide, clozapine
- Ergot derivatives: dihydroergotamine, ergotamine, methylergonovine
- HMG-CoA reductase inhibitors: lovastatin, simvastatin
- Cyclic nucleotide-gated (HCN) channel blockers: ivabradine
- PDE5 inhibitor: sildenafil (Revatio®) when used for pulmonary arterial hypertension
- Sedatives/hypnotics: triazolam, oral midazolam

University of Liverpool COVID-19 Drug Interaction Tool: COVID-19 Drug Interactions

Contraindications and Interactions (Continued)

Nirmatrelvir and ritonavir are CYP3A substrates. Drugs that induce CYP3A may decrease nirmatrelvir and ritonavir plasma concentrations and reduce PAXLOVID therapeutic effect.

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, nifedipine, 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, ombtiasvir/paritaprevir/ritonavir and dasbuvir, 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.

Additional Information & Resources

	Summary	Links
Pregnancy 	There is no human data on the use of nirmatrelvir during pregnancy. Published studies on ritonavir use in pregnancy have not identified an increase in the risk of major birth defects. There is no available data on the presence of nirmatrelvir in human or animal milk, the effects on the breast-fed infant, or the effects on milk production. Ritonavir may reduce the efficacy of combined hormonal contraceptives.	ACOG Use of Oral SARVS-COV-2 protease inhibitor therapy in pregnancy
Efficacy 	**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%).	Pfizer EPIC-HR, phase 2/3 Trial
Patient Checklist Tool for Prescribers	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.	Patient Eligibility Screening Tool for Prescribers
Fact Sheet for Prescribers	**FDA Emergency Use Authorization for Paxlovid**	FDA EUA for Paxlovid
Fact Sheet for Patients/ Caregivers	**FDA Fact Sheet for Patient, Parents, and Caregivers**	FDA Patient/Caregiver Fact Sheet
Drug Interactions Tool	**University of Liverpool COVID-19 Drug Interaction Tool**	COVID-19 Drug Interactions