COVID-19 Oral Antiviral Treatments

Treatment of mild to moderate symptoms in patients with positive direct viral testing who are at high risk for progression to severe COVID-19 disease. Nirmatrelvir + ritonavir (PAXLOVID™) and molnupiravir have received Emergency Use Authorization (EUA) from the U.S. Food and Drug Administration (FDA).

This document is subject to change to remain congruent with COVID-19 guidelines.

	NIRMATRELVIR + RITONAVIR (PAXLOVID)	MOLNUPIRAVIR (LAGEVRIO™)
Indication	• **FIRST LINE** oral outpatient treatment • ≥12 years of age and ≥40 kg • Must begin within 5 days of symptom onset	• Option for when alternative therapies are not accessible or clinically appropriate • ≥ 18 years of age if alternative options are inaccessible or clinically inappropriate • Must begin within 5 days of symptom onset
Efficacy	• Anticipated to be effective against Omicron • Reduce risk of hospitalization and death by 88% FACT SHEET FOR HEALTHCARE PROVIDERS: EMERGENCY USE AUTHORIZATION FOR PAXLOVID (fda.gov)	• Anticipated to be effective against Omicron • Reduce risk of hospitalization and death by 30% FACT SHEET FOR HEALTHCARE PROVIDERS: EMERGENCY USE AUTHORIZATION FOR MOLNUPIRAVIR (fda.gov)
Dose	GFR ≥60 mL/min nirmatrelvir 300 mg (two 150 mg tablets) + ritonavir 100 mg orally BID for 5 days GFR ≥30 - <60 mL/min nirmatrelvir 150mg + ritonavir 100 mg orally BID for 5 days GFR <30 mL/min Use not recommended **Note:** Packaged as a 5-day blister card with two nirmatrelvir 150 mg tablets (pink) and one ritonavir 100 mg tablet (white) packaged for each dose. Dispensing pharmacy will adjust contents for reduced dose. *Take whole (uncrushed) tablet with or without food*	molnupiravir 800 mg (four 200 mg capsules) orally every 12 hours for 5 days **Note:** Packaged as a 40-count bottle of molnupiravir 200 mg capsules Patient will need to know to take four capsules with each dose *Take whole (uncrushed) capsule with or without food*
Adverse Reactions	Generally well tolerated ≥1% incidence: diarrhea, dysgeusia, hypertension, myalgia	Generally well tolerated ≥1% incidence: diarrhea, nausea, dizziness
Contraindications	• Hypersensitivity to ingredients • Co-administering medications that are highly dependent on CYP3A for clearance or are potent CYP3A inducers (see drug interactions) FACT SHEET FOR HEALTHCARE PROVIDERS: EMERGENCY USE AUTHORIZATION FOR PAXLOVID (fda.gov)	No contraindications have been identified based on the limited available data on the emergency use of molnupiravir authorized under the EUA DO NOT USE in pregnancy
Drug Interactions	• Medications that significantly inhibit or induce CYP3A • See Drug Interaction Guide below	None have been identified based on current data
Special Populations	• Not recommended for patients with: ▪ uncontrolled or untreated **HIV-1 infection** ▪ **severe hepatic impairment** (Child-Pugh Class C) ▪ **severe renal impairment** (GFR <30 and dialysis) • No available human data for use in **pregnancy** and **lactation** • Patients on ritonavir or cobicistat containing HIV or HCV regimens should continue regimen as indicated	• **Pregnancy**: DO NOT USE • Women of child-bearing potential should use a reliable method of contraception during treatment and for 4 days after completion • Males should use a reliable method of contraception during treatment and for at least 3 months after last dose • **Lactation:** passes into breastmilk. Pause breastfeeding during treatment and 4 days after treatment.

PAXLOVID Drug Interaction Guide

Ritonavir is an inhibitor, inducer and substrate of various drug-metabolizing enzymes and/or drug transporters. Its ability to inhibit cytochrome P450 (CYP) 3A4 is why it is co-formulated with nirmatrelvir**: ritonavir boosts nirmatrelvir's exposure to a concentration that is effective against COVID-19 and allows for every 12-hour dosing**.

Ritonavir's strong CYP 3A inhibition may increase the concentration of certain concomitant medications, leading to the potential for **significant drug toxicities**. This CYP3A inhibition typically resolves 3-5 days **after** the drug is discontinued but medications with long half-lives whose metabolism is inhibited by ritonavir may be affected longer. Ritonavir's induction properties are less likely to be clinically relevant than when the drug is used chronically for HIV.

Below is a table to help guide the prescriber in assessing for drug interactions but deviation from these recommendations may be appropriate in certain clinical scenarios. **Providers should exercise clinical judgement and consider consultation with the appropriate specialist providers for patients receiving highly specialized drugs, such as antineoplastic and immunosuppressant agents.** To help identify and manage drug interactions, providers should use the EUA fact sheet for PAXLOVID and Liverpool COVID-19 Drug Interactions website.

CONTRAINDICATED: Prescribe an alternative COVID-19 therapy for patients who are receiving any of the medications listed	**PRECAUTION: Before prescribing, determine whether the patient is receiving any of the medications listed** If the patient is receiving any of these medications, providers should exercise clinical judgement which may include continuation of therapy with monitoring, dosage adjustment, withholding therapy as appropriate, or consider using alternative concomitant medication or COVID-19 therapy.		
Drugs highly dependent on CYP3A for clearance: • Alfuzosin • Amiodarone • **Apixaban** • Bosentan • Cisapride • **Clopidogrel** • Clozapine • Colchicine in patients with renal and/or hepatic impairment • Disopyramide • Dofetilide • Dronedarone • Eplerenone • Ergot derivatives • Flecainide • Flibanserin • Glecaprevir/pibrentasvir • Ivabradine • **Lovastatin** • Lumateperone • Lurasidone • Mexiletine • Pethidine • Pimozide • Piroxicam • Propafenone • Propoxyphene • **Quetiapine** • Quinidine • Ranolazine • Rifapentine • **Rivaroxaban** • Sildenafil or Tadalafil for pulmonary hypertension • **Simvastatin** • Ticagrelor • Vorapaxar **Drugs that are potent CYP3A inducers where significantly reduced nirmatrelvir or ritonavir plasma concentrations may be associated with potential for loss of virologic response and possible resistance:** • Apalutamide • Carbamazepine • Phenobarbital • Phenytoin • Rifampin • St. John's Wort	• Alprazolam • Anticancer drugs • Antifungals • Anti-HIV and Anti-HIV protease inhibitors[a] • Atorvastatin • Avanafil • Bedaquiline • Bepridil • Bupropion • Calcium channel blockers • Clarithromycin • Clonazepam • Codeine	• Cyclosporine • Diazepam • Digoxin • Erythromycin • Ethinyl estradiol[b] • Everolimus • Fentanyl • Hepatitis C direct acting antivirals • Hydrocodone • Lidocaine (systemic) • Lomitapide • Lurasidone • Meperidine • Methadone • Midazolam (oral) • Oxycodone	• Propoxyphene • Rifabutin • Rivaroxaban • Rosuvastatin • Salmeterol • Sildenafil for ED • Silodosin • Sirolimus • Suvorexant • Systemic corticosteroids • Tacrolimus • Tadalafil for ED • Tamsulosin • Tramadol • Trazodone • Triazolam • Warfarin

[a] People with HIV should continue their HIV treatment, including those on ritonavir- and cobicistat containing HIV regimens, without interruption during PAXLOVID therapy.
[b] The EUA for ritonavir-boosted nirmatrelvir suggests that individuals who use products containing ethinyl estradiol for contraception should use a backup, non-hormonal contraceptive method because ritonavir-boosted nirmatrelvir has the potential to decrease ethinyl estradiol levels.

Eligibility Criteria

- ☐ Have tested positive for COVID-19 and have had symptoms for 5 days or less.
- ☐ Are at high risk for progression to severe COVID-19, including hospitalization or death.

Please refer to NYS Department of Health information on oral antivirals for COVID-19 for the most up to date guidance.

Oral Antivirals | Department of Health (ny.gov)
https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html

Dispensing Pharmacies

Dispensing is restricted to participating pharmacies only.

Check for HHS Online Tracker for local availability of oral antiviral therapy by entering the zip code. The data displayed in the locator is based on stock on hand as reported by the location and is not a guarantee of availability.

COVID-19 Therapeutics Locator: https://covid-19-therapeutics-locator-dhhs.hub.arcgis.com/

Additional Information

The dispensing pharmacy may not have access to patient information, consider the following:

- ✓ Consider having a staff member contact the pharmacy to ensure product availability before prescribing
- ✓ Provide pharmacy with an up-to-date medication list to prevent severe drug-drug interactions
- ✓ Provide pharmacy with eGFR to appropriately dose PAXLOVID (when e-prescribing include eGFR in directions for non-EPIC users)

Prescriber is encouraged to include a note to the pharmacist in the prescription stating:

- Please fill prescription by _____[insert date]_____.
- This prescription fill by date is within 5 days from symptom onset and complies with the patient eligibility criteria under the EUA.

If a patient has difficulty swallowing large tablets (e.g. potassium ER tabs), then he/she may struggle with Paxlovid (oval shaped, almost an inch long).

If a patient needs to go into the hospital for worsening symptoms or another condition, counsel them to bring Paxlovid with them for continued administration while there.

If you would like additional information on this topic, feel free to contact one of our Ambulatory Care Clinical Pharmacists at AmbulatoryPharmacistTeam@rochesterregional.org or GRIPA.Medical@rochesterregional.org

References:
1.Fact Sheet for HCP: Paxlovid; 2.Fact Sheet for HCP: Molnupiravir; 3.Oral Antivirals | Department of Health (ny.gov); 4.Prioritization of Therapeutics | COVID-19 Treatment Guidelines (nih.gov); 5.https://files.covid19treatmentguidelines.nih.gov/guidelines/covid19treatmentguidelines.pdf;
6.https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/

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