Pharmacy Pearls

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COVID-19 Antivirals: Paxlovid™ & molnupiravir

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Introduction

- Two oral COVID-19 antiviral therapies have received Emergency Use Authorization from the U.S Food and Drug Administration (FDA): **Paxlovid™ (Pfizer)** and **molnupiravir (Merck)**
- **Purpose of treatment** → to decrease complications and progression to severe COVID-19 infection
    - NOT intended to prevent or cure COVID-19 infection
- There is a very limited supply of these agents at local pharmacies and the New York State Department of Health has identified 1-2 pharmacies within each jurisdiction to dispense the medication
    - NOT all pharmacies will have them available to dispense to patients

Place in Therapy + Indication for Use

- Treatment is most effective when given as soon as possible but no more than 5 days after symptom onset
    - High-risk patients who present within 6-10 days of symptom onset should be referred for monoclonal antibody therapy
- Oral antiviral therapy is authorized for patients who:
    - Test positive for SARS-CoV-2 on nucleic acid amplification test or antigen test
    - Have mild-to-moderate COVID-19 symptoms, not hospitalized for severe or critical COVID-19
    - Able to start therapy within 5 days of symptom onset
    - Have a medical condition or other factors that increase their risk for severe disease
- Oral antivirals are not currently authorized for pre-exposure or post-exposure prophylaxis for prevention of COVID-19

Clinical Data

Nirmatrelvir + Ritonavir (Paxlovid™)

EPIC-HR trial

- 2246 unvaccinated, outpatient, COVID-19 positive adults with at least one risk factor for severe disease
- Nirmatrelvir/ritonavir administered within five days of symptom onset, reduced the risk of hospitalization or death at 28 days by **88%** versus placebo (0.8% vs. 6.3%, $p < 0.0001$)
- NNT = 19

Molnupiravir (Lagevrio)

Bernal et al.

- 1433 unvaccinated, outpatient, COVID-19 positive adults with at least one risk factor for severe disease
- Molnupiravir administered within five days of symptom onset
- Reduced the risk of hospitalization or death through day 29 by **31%** versus placebo (6.8% vs. 9.7%, HR 0.69, 95% CI 0.48-1.01)
    - *Did not achieve statistical significance*
- NNT = 35

Dosing and Therapy Considerations

	Nirmatrelvir + Ritonavir (Paxlovid™)	Molnupiravir (Lagevrio)
Dosing	Nirmatrelvir 300 mg + Ritonavir 100 mg BID x 5 days	800 mg every 12 hours x 5 days
Renal Dose Adjustments	eGFR ≥ 60 mL/min: no dosage adjustments eGFR ≥30 to <60 mL/min: nirmatrelvir 150 mg + ritonavir 100 mg BID eGFR <30 mL/min: use is not recommended	No renal dose adjustments necessary
Age	12 years + (weight at least 40 kg, 88 lbs.)	18 years +
MOA	Nirmatrelvir blocks the activity of the SARS-CoV-2-3CL protease, an enzyme required for viral replication, and ritonavir slows the metabolism of nirmatrevir so it remains active in the body for longer	Malnupiravir is a nucleoside analogue that inhibits SARS-Co-V-2 replication
Side Effects	- Dysgeusia (6%), diarrhea (3%), hypertension (1%), myalgia (1%)	- Diarrhea (2%), nausea (1%), dizziness (1%)
Cautions	- **Significant drug interactions** - Consider risk of causing HIV protease inhibitor resistance in patients with uncontrolled/untreated HIV	- **Contraindicated during pregnancy** and lactation (animal studies demonstrate fetal developmental abnormalities) - Avoid use of molnupiravir in patients of childbearing potential, unless other options are not available - Contraindicated in patients <18 years old due to bone and **cartilage toxicity**
Prescribing Considerations	- Dispensed in a 5-day co-packaged blister pack - Patients on ritonavir or cobicistat containing HIV or HCV regimens should continue regimen as indicated	- Advise females of childbearing potential to use reliable contraception during and for four days following therapy - Advise males to use a reliable method of contraception during and for at least three months following therapy
	After initiation of treatment, if hospitalization is required, completion of the 5-day course is at the HCP's discretion	

Paxlovid™: Drug Interactions

Nirmatrelvir/Ritonavir (Paxlovid™) is a CYP3A4 inhibitor, therefore co-administration is contraindicated with:

1. **Potent CYP3A inducers** – may reduce levels of nirmatrelvir and/or ritonavir, resulting in loss of efficacy or resistance
   - Common: arbamazepine, phenobarbital, phenytoin, rifampin, St. John's Wort*
2. **Drugs highly dependent on CYP3A4 for clearance** – may elevate levels of common metabolites
   - Common: piroxicam, amiodarone, colchicine, clozapine, lurasidone, lovastatin, simvastatin, triazolam, ranolazine, alfuzosin*

**This is not a comprehensive list of all possible drug interactions with Paxlovid™, consult the FDA Facts Sheet for more information*

Pharmacy Locator

Oral antiviral locator can be accessed here: https://covid-19-therapeutics-locator-dhhs.hub.arcgis.com/

Note that pharmacies can opt-out of displaying stock