Keeping Up With COVID
Therapeutics Part 2 - Oral Antivirals

Nirmatrelvir/ritonavir (Paxlovid)

Mechanism of Action

- Nirmatrelvir inhibits SARS-CoV-2 main protease (Mpro) rendering it incapable of processing polyprotein precursors, preventing viral replication. Ritonavir is a booster, slowing metabolism of nirmatrelvir

Indication

- **Treatment** of mild-moderate disease in adults and pediatrics (**≥12 years**, weighing at least 40 kg) with positive COVID-19 test result, and who are **at high risk** for severe disease progression (hospitalization or death)
- Not for use in hospitalized patients with **severe** infection

Dosage/Administration (adults and peds)

- Copackaged as nirmatrelvir 150mg and ritonavir 100mg tablets
    - 300mg nirmatrelvir plus 100mg ritonavir orally twice daily for 5 days (no regards to food)
    - Initiate ASAP, but within 5 days of symptom onset
    - Moderate renal impairment: 150mg nirmatrelvir plus 100mg ritonavir twice daily
    - Prescriptions should specify the **numeric dose of each active ingredient**
    - Instruct patients that the pharmacist will alter their daily blister cards to ensure they receive the correct dose

Warnings/Precautions

- TON of CYP3A drug interactions
- Caution with preexisting liver conditions - hepatic transaminase elevations, clinical hepatitis and jaundice (ritonavir)
- Risk of developing resistance to HIV protease inhibitors if uncontrolled/undiagnosed HIV-1
- No dose adjustment for mild renal impairment (eGFR >60 to <90 ml/min)
- Moderate renal impairment (eGFR 30-60 ml/min) – dose adjustment
- NOT recommended for severe renal impairment (eGFR <30 ml/min)

Pregnancy/Lactation

- Unavailable/insufficient data

Molnupiravir

Mechanism of Action

- Metabolized by cytidine nucleoside analogue, NHC, which distributes into cells where NHC is turned into its active form (NHC-TP); NHC-TP incorporates into SARS-CoV-2 RNA by viral RNA polymerase resulting in accumulation of errors in the viral genome, leading to inhibition of replication

Indication

- **Treatment** of mild-moderate disease in **adults** (**18 years or older**) with positive COVID-19 test result, and those who are at **high risk** for severe disease progression (hospitalization or death)
- Not for use in hospitalized patients with **severe** infection

Dosage/Administration

- 800mg orally twice daily for 5 days (no regards to food)
- Initiate ASAP, but within 5 days of symptom onset

Warnings/Precautions

- Not expected to have effect on renal or hepatic impairment

Pregnancy/Lactation

- **Black Box Warning:** based on animal reproduction studies, may cause fetal harm
- Weigh risks and benefits since there are risks associated with untreated COVID-19 in pregnancy
- Not authorized for patients <18 years old due to possible effects on bone/cartilage growth
- No data on lactation; considering alternatives to breastfeeding

Considerations for implementation

1. Practice Model
    a. Ability to confirm patient is positive for COVID-19
    b. Refer patients to dispensing site
    c. Send prescription to pharmacy
    d. Dispense directly from provider office if facility has "physician selling controlled substances facility" permit
2. Storage
3. Billing
    - Third party Insurance
    - HRSA COVID-19 Claims Reimbursement
    - HRSA FAQs

For providers wishing to dispense from practice site (pharmacy, providers office, ect):

1. Ensure facility has appropriate permit (pharmacy license, physician selling controlled substances facility permit)
2. Complete enrollment survey
3. Review compliance and reporting requirements

For pharmacies participating in the Federal Retail Pharmacy Partners (FRPP) program, please contact your FRPP contact for information on how to obtain these therapeutics.

Resources

VDH COVID-19 Therapeutics

VDH COVID-19 Treatment Locator Tool

PAXLOVID Fact Sheet for Healthcare Providers

Molnupiravir Fact Sheet for Healthcare Providers