# Prescribing Oral Antivirals for COVID-19 Treatment

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*Information accurate as of May 23, 2022*

# This presentation is intended for health care providers & pharmacists.



*Information accurate as of May 23, 2022*

# Oral Antivirals for COVID-19

- The U.S. Food & Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for Paxlovid (Nirmatrelvir and Ritonavir) and Lagevrio (Molnupiravir)
- Paxlovid and Lagevrio are not FDA-approved medications in the United States



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# Nirmatrelvir and Ritonavir

## PAXLOVID



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# Paxlovid Eligibility

- Paxlovid is an investigational medicine used to treat mild-to-moderate COVID-19 in adults and children [12 years of age and older weighing at least 88 pounds (40 kg)] with:
  - Positive results of SARS-CoV-2 viral PCR or antigen testing, and
  - High risk for progression to severe COVID-19, including hospitalization or death, and
  - Experiencing mild to moderate COVID-19 symptoms



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# Oral Antiviral Eligibility Criteria

- Comorbidities* may put individuals at an increased risk for severe disease:
  - Cancer
  - Chronic lung diseases
  - Chronic kidney disease
  - Chronic liver disease
  - Diabetes
  - Heart conditions
  - Immunocompromised
  - Overweight/Obese
- Other eligibility considerations:
  - Older age
  - Smoking
  - COVID-19 vaccination (Not fully vaccinated)

*See the CDC website on extra precautions for people with medical conditions. Healthcare providers should consider the benefit-risk for an individual patient: https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html

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# Paxlovid Safety & Effectiveness

- Paxlovid is still being studied
- There is limited information about the safety and effectiveness of using Paxlovid to treat people with mild-to-moderate COVID-19



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# Data on Paxlovid Efficacy: EPIC-HR*

- Phase 2/3 double-blind study in 2,246 non-hospitalized, symptomatic adults with a laboratory-confirmed SARS-CoV-2 infection who were randomized 1:1 to receive Paxlovid™ or placebo for 5 days
- Population:
  - Enrolled within 5 days of symptom onset
  - ≥1 risk factor for progression to severe disease
  - No prior COVID-19 vaccine receipt or prior COVID-19 infection
  - Standard of care treatment allowed, but the primary analysis population was limited to subjects who did not receive COVID-19 monoclonal antibodies (mAbs)
- 98% of SARS-CoV-2 variants identified in EPIC-HR were Delta

*More information about the study EPIC-HR: https://clinicaltrials.gov/ct2/show/NCT04960202

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# Data on Efficacy: EPIC-HR

**Efficacy Results in Non-Hospitalized Adults with COVID-19 Dosed within 5 Days of Symptom Onset who Did Not Receive COVID-19 mAb Treatment at Baseline**

| | PAXLOVID™ (N=1,039) | PLACEBO (N=1,046) |
|---|---|---|
| Primary endpoint: COVID-19 related hospitalization or death from any cause through Day 28, n(%) | 8 (.08%) | 66 (6.3%) |
| Reduction relative to placebo for primary endpoint[a] [95%, CI], % | -5.62 (-7.21,-4.03) | |
| All-cause mortality through Day 28, % | 0 | 12 (1.1%) |

a. The estimated cumulative proportion of participants with COVID-19 related hospitalization or death from any cause through Day 28 was calculated for each treatment group using the Kaplan-Meier method, where subjects without hospitalization and death status through Day 28 were censored at the time of study discontinuation.

- **88% (95% CI: 75%, 94%)** relative risk reduction for the primary endpoint (proportion of subjects with COVID-19 related hospitalization or death from any cause through Day 28)
- Treatment effect was generally consistent across subgroups, including baseline serology status

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# Paxlovid Contraindications

- People with allergies to nirmatrelvir, ritonavir, or any of the ingredients in Paxlovid should NOT take this medication
- Co-administration with potent CYP3A4 inducers or drugs highly dependent on CYP3A4 for clearance



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# People who are taking any of the following medicines should NOT take Paxlovid

- Alfuzosin
- Pethidine, propoxyphene
- Ranolazine
- Amiodarone, dronedarone, flecainide, propafenone, quinidine
- Colchicine
- Lurasidone, pimozide, clozapine
- Dihydroergotamine, ergotamine, methylergonovine
- Lovastatin, simvastatin
- Sildenafil (Revatio®) for pulmonary arterial hypertension (PAH)
- Triazolam, oral midazolam
- Apalutamide
- Carbamazepine, phenobarbital, phenytoin
- Rifampin
- St. John's Wort (hypericum perforatum)

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# Other Paxlovid Interactions

- Anticoagulants
- Anticancer drugs
- Antifungals
- Calcium channel blockers
- Cardiac glycosides (digoxin)
- HIV medications
- HMG-CoA reductase inhibitors (Statins)
- Hormonal contraceptives*
- Immunosuppressants
- Systemic corticosteroids

NOT a comprehensive list – providers should consult appropriate references before prescribing

*Hormonal contraceptives may be less effective while taking Paxlovid. Patients should be counseled to use a back-up method of contraception.

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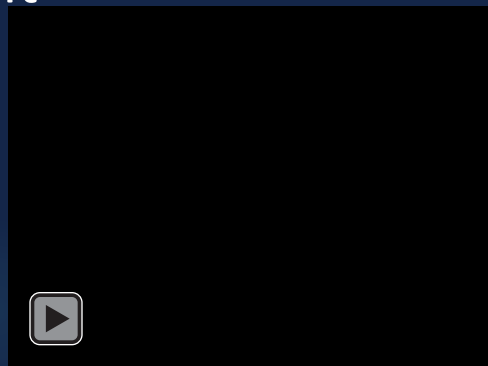

# Checking for Paxlovid Drug Interactions

Resources:

- Lexicomp
- Micromedex
- Clinical Pharmacology
- Epocrates (free version available)

Double Check:

- Medications will also be screened for interactions at the pharmacy



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# Paxlovid Warnings/Precautions

- Risk of serious adverse reactions due to drug interactions
- Allergic reactions/hypersensitivity
- Hepatotoxicity
- Risk of HIV-1 resistance development



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# Paxlovid Side Effects

- Altered sense of taste (6%)
- Diarrhea (3%)
- High blood pressure (1%)
- Muscle aches (1%)



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# Paxlovid with Renal Impairment

- Systemic exposure of nirmatrelvir increases in renally impaired patients
- Mild renal impairment (eGFR ≥60): No dosage adjustment
- Moderate renal impairment (eGFR ≥30 to <60 mL/min): Reduce nirmatrelvir dose from 300 mg to 150 mg
- Severe renal impairment (eGFR <30): Paxlovid not recommended



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# Paxlovid with Hepatic Impairment

- No dosage adjustment for mild or moderate hepatic impairment
- Paxlovid is not recommended in severe hepatic impairment
- Hepatic transaminase elevations, clinical hepatitis, and jaundice have occurred in patients receiving ritonavir
  - Caution should be exercised when administering Paxlovid to patients with pre-existing liver diseases, liver enzyme abnormalities, or hepatitis



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# Paxlovid during Pregnancy

- There is no experience treating pregnant women or breastfeeding mothers with Paxlovid
- For a mother and unborn baby, the benefit of taking Paxlovid may be greater than the risk from the treatment
- Patients on oral contraceptive therapy should use an alternative or additional nonhormonal form of contraception as a back-up method while taking Paxlovid
- Breastfeeding patients should discuss options and specific situation with a healthcare provider



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# Paxlovid Dosing

- **Nirmatrelvir 300 mg** (two 150 mg tablets) and **ritonavir 100 mg BID for 5 days**, without regard to food
- Renal dose adjustment: nirmatrelvir 150 mg and ritonavir 100 mg BID for 5 days
- Nirmatrelvir co-packaged with ritonavir in 5 daily dose blister cards
- Paxlovid should be started as soon as possible after diagnosis of COVID-19, and within 5 days of symptom onset
- Completion of the full 5-day treatment course is important to maximize viral clearance and minimize transmission of SARS-CoV-2



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# Molnupiravir

## LAGEVRIO



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# Molnupiravir Eligibility

- Molnupiravir (MOV) is authorized for the treatment of mild-to-moderate coronavirus disease 2019 (COVID-19) in adults 18 years or older with:
  - Positive results of SARS-CoV-2 viral PCR or antigen testing, and
  - High risk* for progression to severe COVID-19, including hospitalization or death, and
  - Experiencing mild to moderate COVID-19 symptoms, and
  - Alternative COVID-19 treatment options authorized by FDA are not accessible or clinically appropriate
- Molnupiravir is not as effective as nirmatrelvir/ritonavir (Paxlovid)
  - Molnupiravir may be considered in patients who should not take Paxlovid due to drug interactions or severe renal or hepatic impairment, or if Paxlovid is not available

*See the CDC website on extra precautions for people with medical conditions. Healthcare providers should consider the benefit-risk for an individual patient: https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html

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# Data on Molnupiravir Efficacy: MOVe-OUT

- Phase 2/3 randomized, placebo-controlled, double blind clinical study to evaluate MOV in non-hospitalized adults with COVID-19
- Outpatient adults with mild or moderate COVID-19
  - Laboratory-confirmed SARS-CoV-2 infection with sample collection and onset of COVID-19 symptoms ≤5 days prior to randomization
- All participants at increased risk for severe illness from COVID-19
  - >60 years of age, active cancer, CKD, COPD, obesity (BMI ≥ 30), serious heart conditions (CAD, heart failure, cardiomyopathies), DM
- SARS-CoV-2 vaccines were prohibited any time prior to randomization and through Day 29
- Pregnant individuals excluded and contraception was required

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# Data on Molnupiravir Efficacy: MOVe-OUT

| | Molnupiravir (N=709) n(%) | Placebo (N=699) n(%) | Adjusted Risk Difference % (95%CI) |
|---|---|---|---|
| **All-cause hospitalization ≥24 hours for acute care or death through Day 29** | 48 (6.8%) | 68 (9.7%) | -3.0 (-5.9%, -0.1%) |
| **All-cause mortality through Day 29** | 1 (0.1%) | 9 (1.3%) | |

- *The determination of primary efficacy (percentage of participants who were hospitalized or died through day 29 due to any cause) was based on a planned interim analysis of 762 subjects. At the interim analysis, 7.3% of participants who received molnupiravir were either hospitalized or died through Day 29 (28/385), compared with 14.1% of placebo-treated participants (53/377). The adjusted risk difference was -6.8% with a 95% CI of (-11.3%, -2.4%) and 2-sided p-value = 0.0024.
- **Adjusted relative risk reduction of molnupiravir compared to placebo for all randomized participants was 30% (95% CI: 1%, 51%).**
- Analyses are adjusted by the stratification factor of time of COVID-19 symptom onset (≤3 days vs. >3 [4-5] days).



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# Molnupiravir Side Effects

- Diarrhea (2%)
- Nausea (1%)
- Dizziness (1%)



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# Molnupiravir During Pregnancy

- MOV is not recommended for use during pregnancy
  - Based on animal data, MOV may cause fetal harm (embryo-fetal toxicity) when administered to pregnant individuals
- If a healthcare provider determines that the benefits outweigh the risks for an individual pregnant patient, they must:
  - Counsel the patient regarding the known and potential benefits and potential risks of MOV use during pregnancy
  - Document that the patient is aware of the known and potential benefits and potential risks of MOV use during pregnancy
  - Make the individual aware of the pregnancy surveillance program
    - If the pregnant individual agrees to participate in the pregnancy surveillance program and allows the prescribing healthcare provider to disclose patient specific information to Merck, the prescribing healthcare provider must provide the patient's name and contact information to Merck
    - 1-877-888-4231 or https://pregnancyreporting.msd.com

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# Molnupiravir: What Clinicians Need to Know

- Molnupiravir is not authorized for use in patients < 18 years of age
  - May affect bone and cartilage growth
- Oral antivirals may be used regardless of COVID-19 vaccination status
- Breastfeeding is not recommended during treatment with molnupiravir and for 4 days after the final dose
- No drug interactions have been identified with molnupiravir based on the limited available data
- No dosage adjustment is recommended in patients with any degree of renal or hepatic impairment



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# Molnupiravir Dosing

- **800 mg** (four 200 mg capsules) taken orally **every 12 hours for 5 days**, with or without food
- Take as soon as possible after a diagnosis of COVID-19 has been made, and within 5 days of symptom onset
- Completion of the full 5-day treatment course is important to maximize viral clearance and minimize transmission of SARS-CoV-2



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# ECDOH Test to Treat

- Started program in April 2022
- Available to symptomatic people with a positive COVID-19 rapid test at ECDOH test sites
  - Patients are told they should contact their primary care provider for a prescription
  - If cannot contact a primary care provider, patients may consider participating in Erie County Test to Treat program
  - Consented patients are screened by pharmacist
  - If eligible, ECDOH medical provider sends Rx to participating pharmacy near patient
  - Cost of prescription is covered either by patient's insurance or federal government



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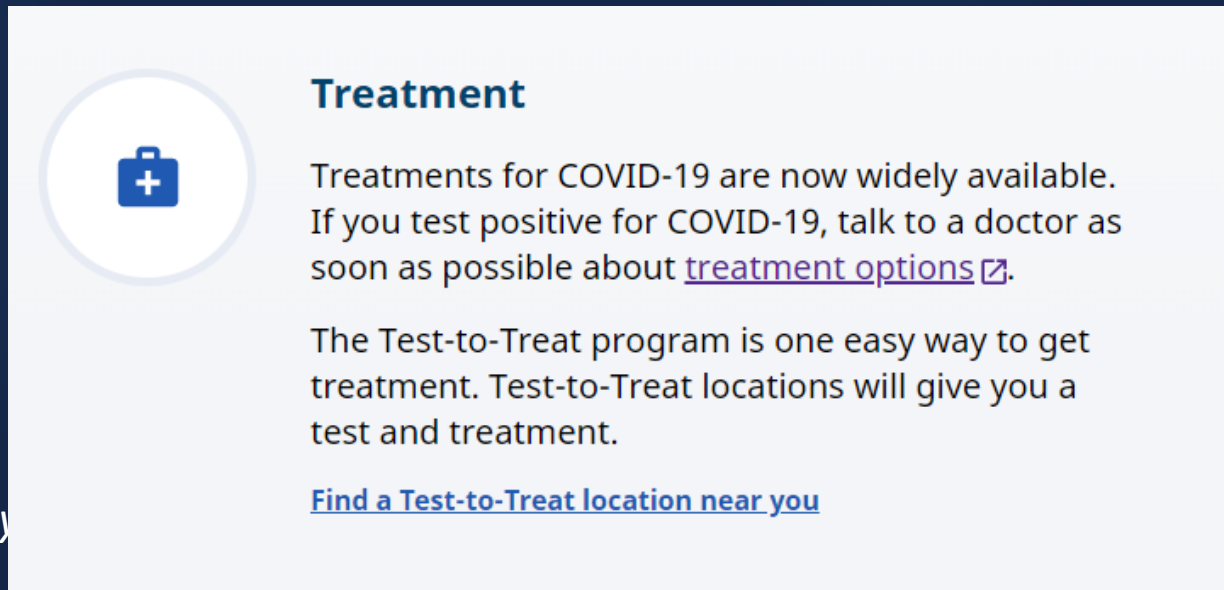
# Pharmacy Availability

- Searchable map at covid.gov lists Test-to-Treat locations and pharmacies with medications available

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# Test to Treat

- ECDOH sites provide COVID-19 tests to a fraction of the Erie County residents who are tested in any given week
- **The community needs support from local providers** to screen and prescribe COVID-19 treatment to eligible patients



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# COVID-19 Vaccination

- Web Site
  - www.erie.gov/vax
- Social media
  - Twitter: @ecdoh
  - Facebook (Erie County Department of Health)
  - Instagram (@eriecohealth)
  - Erie County, NY Youtube Channel
    www.youtube.com/eriecountyny



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# Erie County Resources

- **www.erie.gov/covid19**
  - COVID-19 Info Line: (716) 858-2929
- **www.erie.gov/covidmap**
  - Data visualization: case counts, ZIP code and municipality maps
- **www.erie.gov/vax**
  - Vaccine clinic schedule

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