

Oral Antiviral Treatment for COVID-19

Key Messages

- The oral antiviral medications Molnupiravir and Paxlovid have received FDA emergency use authorizations for the treatment of mild- to-moderate COVID-19 in patients who are at high risk for progression to severe COVID-19, including hospitalization or death.
- These medications are now available at some [LA County locations](#) and these [Orange County locations](#) including pharmacies and clinics. As supplies are currently very limited, providers/patients should call ahead to check that product is available.
- For information about how to access this therapy for your patients, visit the LAC DPH [COVID-19 Monoclonal & Antiviral Therapy for Non-Hospitalized Patients](#) webpage. The webpage also includes information about other treatments for non-hospitalized patients.
- Providers are asked to identify and inform high risk patients in advance regarding the availability of these medications so that if they become infected, treatment can be started as soon as possible and within 5 days of symptom onset.

The information below is taken from California Department of Public Health (CDPH) recommendations for providers.

Background Information

- Paxlovid (nirmatrelvir tablets and ritonavir tablets, co-packaged for oral use) is an oral protease inhibitor. Pfizer announced the results from a trial of 2,246 adults who received either Paxlovid or placebo. All patients had not received a COVID-19 vaccine and had not been previously infected with COVID-19. In the study, Paxlovid significantly reduced the proportion of people with COVID-19 related hospitalization or death from any cause by 88% compared to placebo among patients treated within five days of symptom onset. Paxlovid has received an EUA authorizing use for the treatment of mild-to-moderate COVID-19 in patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death.
 - Paxlovid (Pfizer) — nirmatrelvir tablets and ritonavir tablets, co-packaged for oral use. If normal renal function, 300 mg nirmatrelvir (two 150 mg tablets) with 100 mg ritonavir (one 100 mg tablet), with all three tablets taken together twice daily for 5 days. Treatment started as soon as possible after diagnosis of COVID-19 and within 5 days of symptom onset. If possible write electronic prescription through EPIC to a pharmacy but if not possible, write paper prescription and give to patient with instructions on where to go and how to take the medication.

The challenge with Paxlovid is the possible drug drug interactions with medications that patients are already taking. The Paxlovid EUA statement has a list of drugs that may interact.

- Molnupiravir is a nucleoside analogue that inhibits SARS-CoV-2 replication by viral mutagenesis. Merck announced results from a trial of 1,433 patients. Enrolled participants had not received a COVID-19 vaccination and had at least one risk factor associated with poor disease outcomes and symptom onset within five days prior to study enrollment. The risk of hospitalization for any cause or death through day 29 was lower with Molnupiravir (6.8%) than

with placebo (9.7%), for a relative risk reduction of 30%. Molnupiravir is authorized for treatment of mild-to-moderate COVID-19 in adults with positive results of direct SARS-CoV-2 viral testing who are at high risk for progressing to severe COVID-19, including hospitalization or death, and for whom alternative COVID-19 treatment options authorized by FDA are not accessible or clinically appropriate.

- Molnupiravir (Merck) — 800 mg (four 200 mg capsules) taken orally every 12 hours for 5 days. Treatment started as soon as possible after diagnosis of COVID-19 and within 5 days of symptom onset. If possible write electronic prescription through EPIC to a pharmacy but if not possible, write paper prescription and give to patient with instructions on where to go and how to take the medication.

The drawbacks with Molnupiravir is that it may cause cancer causing mutations in human DNA. We don't know the short or long term consequences of this medication so I would only use it in elderly individuals that are highly immune suppressed or unvaccinated.

Instructions to Providers

Both oral antivirals may only be prescribed for an individual patient by physicians, advanced practice registered nurses, and physician assistants that are licensed or authorized under state law to prescribe drugs in the therapeutic class to which Paxlovid and Molnupiravir belong (i.e., anti-infectives).

Providers should carefully review the fact sheet for healthcare providers (available both for [Paxlovid](#) and [Molnupiravir](#)) before prescribing either medication to ensure that the patient's condition warrants treatment, that there are no drug interactions, and that there are no contraindications to therapy.

The use of Molnupiravir is not recommended for anyone of child bearing age including men and Paxlovid may lead to a risk of HIV-1 developing resistance to HIV protease inhibitors in individuals with uncontrolled or undiagnosed HIV-1 infection.

Unfortunately, supply of both oral antivirals is expected to be limited. **Providers should communicate with pharmacies to ensure that supply exists before sending patients to pick up prescriptions.**

Patients meeting the below criteria may be eligible for treatment with Paxlovid or Molnupiravir:

- Patients who are *symptomatic* with mild to moderate COVID-19 AND
- Have positive results of direct SARS-CoV-2 viral testing AND
- Are at *high risk* for progressing to severe COVID-19 and/or hospitalization AND
- Are within 5 days from the start of their symptoms

The definition of mild and moderate disease and defined by NIH is below:

- *Mild Illness*: Individuals who have any of the various signs and symptoms of COVID-19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) but who do not have shortness of breath, dyspnea, or abnormal chest imaging.
- *Moderate Illness*: Individuals who show evidence of lower respiratory disease during clinical assessment or imaging and who have an oxygen saturation (SpO2) $\geq 94\%$ on room air at sea level.

Neither oral option is authorized for treatment in patients requiring hospitalization due to severe or critical COVID-19.

For a complete list of risk factors for disease progression, including information on the relative risk of severe disease, see the CDC webpage [Underlying Medical Conditions Associated with High Risk for Severe COVID-19](#).

Treatment should be prioritized in unvaccinated or incompletely vaccinated individuals and vaccinated individuals who are not expected to mount an adequate immune response (e.g., individuals who are immunocompromised or on immunosuppressive medications or individuals aged ≥65 years).

Currently, supply remains limited after applying the above criteria, CDPH recommends additionally prioritizing high-risk patients with *moderate illness* as defined above in the following order:

1. Immunocompromised or on immunosuppressive medications
2. Incompletely vaccinated AND > 65 years of age with risk factors for severe disease
3. > 65 years of age with risk factors for severe disease

Molnupiravir is only authorized for use if alternative COVID-19 treatment options authorized by FDA are not accessible or are not clinically appropriate. In cases where Paxlovid or Sotrovimab are not available for treatment and the patient is at high risk, consideration should be given to [Remdesivir IV daily for three days](#) or Molnupiravir can be considered.

Paxlovid or Sotrovimab should be prescribed first and if unavailable and the benefits outweigh the risks of using Molnupiravir, then Molnupiravir can be used. Remdesivir IV daily for three days can also be considered and we are in contact with our infusion companies about obtaining this for our patients as a home health referral similar to monoclonal antibody.

More information

- NIH [COVID-19 Treatment Guidelines](#)
- CDPH Health Alerts for [Paxlovid](#) (12/23/21) and [Molnupiravir](#) (12/24/21)
- LAC DPH provider webpage [COVID-19 Monoclonal & Antiviral Therapy for Non-Hospitalized Patients](#)
- CDPH webpage [SARS-CoV-2 Antiviral Therapeutics](#)

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